

A STUDY TO CORRELATE THE SERUM URIC ACID LEVELS WITH THE DURATION AND SEVERITY OF MIGRAINE

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ABSTRACT

Objectives: The objectives of the study were to assess the serum levels of uric acid in patients of migraine and to correlate the levels of uric acid with duration and severity of migraine.

Methods: This observational study was conducted in patients with complaint of headache, due to migraine who attended neurology and general medicine out patients department of tertiary care teaching hospital of Udaipur, Rajasthan. Uric acid levels were compared between both the genders with respect to age group, frequency of attack, and duration of migraine. Uric acid levels were also correlated with different parameters.

Results: A total of 500 patients were evaluated during the study period of 2 years. Mean uric acid in male patients was 5.02 ± 1.40 mg/dl, and in females it was 4.99 ± 1.39 mg/dl. Uric acid levels in male and female patients were found non-significant across all age groups, with duration of migraine and frequency of migraine attack ($p > 0.05$). There was a significant correlation between uric acid levels and migraine severity in present study ($p < 0.05$), but there was no correlation with age, duration of migraine, and frequency of migraine attacks per month ($p > 0.05$).

Conclusion: The study concluded that uric acid levels are within normal range in all age group as well as either of gender in patients of migraine. Hence, there is no relation between uric acid and duration and frequency of migraine but positive correlation with severity of migraine.

Keywords: Headache, Migraine, Uric acid, Migraine severity.

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INTRODUCTION

Migraine is common in women and has a strong genetic component. There are various types of migraines, and they are identified by the signs and symptoms that a person experiences. Some are triggered by seasonal changes and others by alterations in hormone levels, especially in women. In 1988, the International Headache Society produced a system for classifying migraines, a system also adopted by the World Health Organization [1]. This system was updated in 2004 (The international classification of headache disorders (ICHD-II), in 2013 (ICHD-III) and is the established basis for defining types of headaches. In migraine some patients experience a premonitory phase, which occurs hours or days before the headache, followed by a resolution phase. Hyperactivity, hypoactivity, depression, food cravings, recurrent yawning, and other less common symptoms are recorded during the premonitory and resolution phases. Nearly one-third of migraine patients reported to have 3 or more headache attacks per month, and half of migraine patients have severe impairment in daily functions both at home and at work [2]. 50% of general population suffers from headaches during any given year, and 90% report a lifetime history of headache. The estimated prevalence of headache over periods between 1 month and lifetime in children and adolescents is more than 50% [3]. About 20% of children and adult migraine patients continue to suffer throughout their lives, whereas 50% experience remission over extended periods.

The course of migraine is highly variable. Before adolescence, migraine incidence is modest, but it quickly increases until middle adulthood. It tends to peak in the middle-aged group but is reported to be lower among adolescents and the elderly (aged above 60 years) [2]. The prevalence of migraine is higher in women (5–25%) than in men (2–10%) [2-4]. Individuals with migraines experience diverse symptoms, and these symptoms can change from attack to attack. In addition, migraine attacks can vary in frequency and duration, typically

lasting 4–72 h. Even though people may not experience any symptoms in between attacks, the attacks have a significant negative impact on job, family, and social relationships. Numerous precipitants of migraine attacks have been consistently implicated including hormonal changes, stress or its cessation, fasting, fatigue, oversleeping, particular food and beverages, drug intake chemical additives, bright light, weather changes, and exercise, but these agents/situation have been observed to vary dramatically within and between individuals in prospective research.

Migraine, however, is also known to be comorbid with more than 20 somatic diseases, among which musculoskeletal disorders, including fibromyalgia, are highly prevalent [5]. Comorbidity with psychological disorders including generalized anxiety disorder, panic disorder, and depression is even more widespread [6]. Most daily headache sufferers have both Vitamin D₃ and secondary Vitamin B deficiencies.

Though migraine is treated after proper diagnosis with suitable medical therapy, a few patients are not totally relieved. Hence, studies are done to ascertain its etiology and discover better treatment options. Three parameters, namely, Vitamin B₁₂, Vitamin D₃, and serum uric acid levels in random sample appear to be suitable options for such exploration. Role of Vitamin D₃ and Vitamin B₁₂ in migraine have been reported by various studies [7,8]. Uric acid has been correlated as a risk factor for many neurological conditions. Various studies have shown that migraine frequency is less common in patients of gout [9-11]. Role of uric acid level in migraine patients had not been evaluated much. Hence, this present study was planned to assess the serum levels of uric acid in patients of migraine and to correlate the levels of uric acid with duration and severity of migraine.

METHODS

This observational study was conducted in patients with complaint of headache, due to migraine who attended Neurology and General

Medicine out patients department of tertiary care teaching hospital of Udaipur, Rajasthan. This study was conducted only after approval from institutional ethics committee. Consecutive sampling was done to enroll the patients. All the patients of age more than 10 and <60 years with headache/migraine (primary cause), attending in outpatient-department during the study period were included in the study. Patients with headache due to any other cause other than migraine and other comorbidity causing headache were excluded out.

Procedure

All patients were subjected to detailed history and thorough clinical examination. Demographic details such as name, age, sex, address, and contact information were noted in a pre-structured pro forma. Subjects were also enquired regarding past medical illness which can be a risk factor for migraine. History regarding drugs and other Ayurvedic or naturopathy preparation were noted. Detailed history with signs and symptoms was taken to confirm the cause of headache as migraine. All other causes of headache were ruled out by history, clinical examination and appropriate investigations. Complete blood count and other relevant investigations including serum uric acid were done in all the patients. Further set of investigation were selectively done to confirm the diagnosis and etiology. Immunological profile and NCCT/Magnetic resonance imaging Brain were done in patients as per the primary suspicion.

Uric acid levels were compared between both the genders with respect to age group, frequency of attack and duration of migraine. Uric acid levels were also correlated with different parameters. Migraine severity was assessed with visual analogue scale.

Statistical analysis

Descriptive analysis was done using mean, standard deviation, ratio, and proportion with percentage (%). Results were analyzed by suitable tests using SPSS software and p-value was calculated. A value of p<0.05 was considered statistical significant.

RESULTS

A total of 500 patients were evaluated during the study period of 2 years. Out of total 500 patients, 251 were males and 249 were female patients. In the present study, mean age of male patients was 39.76±10.89 years and of female patients was 40.08±10.83 years. Maximum patients (27.2%) were in the age group of 40-49 years followed by 26% in 30-39 years, 24%, 21%, and 1.2% in age groups 50-59 years, 20-29 years, and 10-19 years, respectively (Table 1).

Mean uric acid in males was 5.02±1.40 mg/dl, and in females it was 4.99±1.39 mg/dl. There was no significant difference between both the groups. (p>0.05) Uric acid levels in male and female patients across all age groups were in normal range. There was also no significant difference between male and female for uric acid level with duration of migraine and frequency of migraine attack (p>0.05) (Table 2).

Migraine severity was higher in females (6.72±6.59) than males (5.52±5.97), but was statistically non-significant. Mean frequency of number of migraine attacks per month was also more in females (9.65±10.89) than males (8.16±10.02), but was statistically non-significant. Mean duration of migraine attack was more in females (17.9±2.3 h) than males (11.7±0.91 h); this result was found to be statistically highly significant (Table 3).

There was a significant correlation between uric acid levels and migraine severity in present study, but there was no correlation with age, duration of migraine and frequency of migraine attacks per month (Table 4).

DISCUSSION

Migraine is a very common disease all over world. Migraines have been tied to concerns ranging from depression to asthma to heart

Table 1: Demographic details of all the patients

| Demographic parameters | Male (n=251) | Female (n=249) |
|------------------------|--------------|----------------|
| | n (%) | n (%) |
| Age (mean±SD) | 39.76±10.89 | 40.08±10.83 |
| Age group (in years) | | |
| 10-19 | 4 (1.59) | 2 (0.80) |
| 20-29 | 51 (20.32) | 54 (21.69) |
| 30-39 | 69 (27.49) | 64 (25.70) |
| 40-49 | 70 (27.89) | 66 (26.51) |
| 50-59 | 57 (22.71) | 63 (25.30) |

Table 2: Uric acid levels in male and female patients with different age groups, with duration of migraine and frequency

| Uric acid levels with different parameters | Uric acid (mg/dl) | | p-value |
|--|-------------------|-----------|---------|
| | Male | Female | |
| | Mean±SD | Mean±SD | |
| Uric acid (mg/dl) | 5.02±1.40 | 4.99±1.39 | 0.83 |
| Age group (years) | | | |
| 10-19 | 5.38±1.23 | 5.25±0.64 | 0.873 |
| 20-29 | 4.85±1.42 | 4.86±1.32 | 0.970 |
| 30-39 | 5.19±1.15 | 5.14±1.57 | 0.835 |
| 40-49 | 5.06±1.42 | 4.80±1.41 | 0.286 |
| 50-60 | 4.89±1.65 | 5.15±1.25 | 0.336 |
| Duration of migraine (years) | | | |
| <5 | 4.93±1.36 | 4.96±1.28 | 0.85 |
| 5-10 | 5.14±1.35 | 5.36±1.35 | 0.43 |
| 10-15 | 4.92±1.64 | 4.88±1.58 | 0.92 |
| 15-20 | 5.65±1.53 | 4.59±1.84 | 0.09 |
| >20 | 5.11±1.43 | 4.92±1.27 | 0.64 |
| Frequency of migraine attacks | | | |
| 0-7 | 5.07±1.43 | 5.05±1.41 | 0.90 |
| 8-14 | 4.94±1.48 | 4.75±1.53 | 0.58 |
| 15-21 | 5.34±0.75 | 5.61±0.85 | 0.52 |
| >21 | 4.87±1.34 | 4.86±1.23 | 0.97 |

Table 3: Duration, severity, and frequency of migraine attacks in both the groups

| Migraine parameters | Male | Female | p-value |
|---------------------------------------|------------|------------|---------|
| | Mean±SD | Mean±SD | |
| Migraine severity | 5.52±5.97 | 6.72±6.59 | >0.05 |
| Frequency (No. of attacks per months) | 8.16±10.02 | 9.65±10.89 | >0.05 |
| Duration of attack (hours) | 11.7±0.91 | 17.9±2.3 | <0.001* |

*significant

Table 4: Correlation of various parameters with uric acid levels

| Parameters | Correlation | |
|--------------------------------------|-------------|---------|
| | "r" value | p-value |
| Age (years) | -0.019 | >0.05 |
| Duration (hours) | -0.010 | >0.05 |
| Frequency (No. of attacks per month) | -0.031 | >0.05 |
| Migraine severity | 0.242 | <0.05* |

*significant

disease [12]. Considering the extensive prevalence and excruciating painful effect of migraine, options for curing, alleviating or mitigating, it needs to be exhaustively explored. Since migraine is impacted by life style, local and socioeconomic condition [12], we planned this study based on the headache patients from underdeveloped and developing region of south west Rajasthan attending tertiary care teaching hospital, Udaipur.

In the present study, both male and female migraine patients were almost equal in number, that is, prevalence was similar in both genders. Most of the patients (51.20%) were above 40 years of age. Mean age of male patients was 39.76±10.89 years and it was 40.08±10.83 years in female patients. Many others studies have also reported similar mean age of migraine patients [13,14]. Most of the studies have earlier proved that migraine is common in female patients [14,15]. Equal incidence of migraine in both genders in the present study could be due to demographic variations.

In the present study, mean uric acid value was 5.02±1.40 mg/dl in male patients and it was 4.99±1.39 mg/dl in females. These values were well within the normal range (male 3.4–7 mg/dl, female 2.4–5.7 mg/dl); and there was also no statistically significant difference in uric acid levels in either gender. Many other studies have also reported non-significant difference in serum uric acid levels between migraine cases and healthy controls [13,16]. We could not find any study which had compared uric acid levels between male and female migraine patients. In one study, uric acid was measured in topiramate treated patients and matched control subjects and found significantly higher uric acid levels in the migraine patients than in healthy controls [17].

Uric acid levels in male and female patients were found non-significant across all age groups, with duration of migraine and frequency of migraine attack. Migraine patients with longer duration of disease and higher frequency in both genders had normal level of uric acid.

Migraine severity and frequency of attack per month were found higher in females but it was non-significant. In the present study, duration of attacks was also significantly more in female patients than males. Various other studies have reported significantly higher migraine severity and frequency of attack in females; and they have also reported duration of attack significantly more in female [18-20]. There was significant correlation between uric acid levels and migraine severity in the present study, but no correlation was found with other factors such as age, duration of migraine, and frequency of migraine attacks per month in both genders. Although many studies have reported that disease duration and the attack frequency are significantly associated with migraine [21], we could not find any study which had correlated level of uric acid with the disease duration and the frequency of attack.

Limitations

MTHFR gene is one of the genetic risk factors for migraine but due to financial constraint the MTHFR gene could not be tested.

CONCLUSION

The study concluded that uric acid levels are within normal range in all age group as well as either of gender in patients of migraine. Hence, there is no relation between uric acid and duration and frequency of migraine but positive correlation with severity of migraine. So in case of severe migraine uric level can be monitored and patient can be treated accordingly.

AUTHORS' CONTRIBUTION

All the authors contributed to the preparation of the final manuscript.

CONFLICTS OF INTEREST

None.

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