# COMPARISON OF PENTRAXIN-3 IN MIGRAINE PATIENTS WITHOUT AURA AND HEALTHY CONTROLS

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**Abstract**

**Background and Objectives:** Migraine is a common cerebrovascular condition marked by one-sided, pulsating headache, which may or may not be accompanied with an aura. Migraine is mostly found in females who are of childbearing age. One of the speculated mechanisms for the pathophysiology of migraine is endothelial dysfunction. A new biomarker of inflammatory disorders, pentraxin-3 is often produced by endothelium injury. In earlier investigations, it was shown that migraine sufferers had elevated levels of pentraxin-3. Our study's objectives were to analyze the serum pentraxin-3 levels in migraine sufferers without aura and healthy controls.

**Methods:** It was a cross-sectional comparative study. This was done at the IMBB Department, University of Lahore, Lahore Pakistan, from March 2020 to April 2022. We took 40 diagnosed migraine cases and 40 healthy controls. Detailed examination was done and proformas were filled by both cases and controls. Serum was collected by each of them and pentraxin-3 values were determined by using specific Elisa kits. SPSS version 22 was used for statistical analysis. For normality of data Shapiro wilk test was used. Mann whiteny U test was used for the comparision of means of pentraxin-3 in migrainers and healthy controls.

**Results:** The data were non-normally distributed after the Shapiro-Wilk Test. The average age of the controls was 25±6.06 years, while that of individuals with migraines was 26±7.78 years. Patients with migraine were mostly women. The majority of the patients had BMI category 18 to 24.5. Patients with migraine had mean pentraxin-3 levels of 145.75 ±157.7 pg/l, compared to 43.65 ±33.01 pg/l in the control group. Median was 100.5 in cases and 31.15 in controls. P-value was 0.0001.

**Conclusion:** When compared to the control group, migraine patients had considerably higher blood levels of PTX-3, and no correlations between age, BMI, marital status, smoking history, and usage of preventative medications were found.

**Key words:** migraine, pentraxin-3, endothelial dysfunction, C-reactive protein (CRP),

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Migraine is a type of headache that is usually unilateral, temporal, throbbing / pulsatile, and cyclical, that may disrupt daily life activities and may last for 4 to 72 hours.[1] Sign and symptoms include photophobia, phonophobia, nausea, vomiting, and some atypical abdominal features. Many factors that trigger migraine are stress, sleep disturbances, weather change, loud noises, intense lights, some specific food and few medications.[2] It is ranked third highest in the world that cause disability in age less than 50 years (both male and female) according to the global burden of disease criteria (GBD2015). Prevalence of migraine headache is high in female as compare to men.[3] Migraine without aura is called common migraine. Migraine can be classified into acute and chronic on the bases of duration of disease. Disability for more than 3 months and attack duration for up to 15 days is considered as chronic migraine. There are four different phases of

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migraine which are distinguished on the bases of sign and symptoms.[4] Prodrome / premonitory phase that occur before headache is considered as phase 1, 2 aura phase that is Sensio neurological deficit with headache ache or without headache, 3 migraine headache phase, and 4 postdrome phase occurs after headache resolution. Sign and symptoms of these phases include increased hypothalamic activity like yawning, anxiety, and craving for food, fatigue, neck stiffness and body aches (ICHD-3 2018).

Migraine is considered as a functional, neurological and genetic disability. Many substances play a significant role in pathophysiology of migraine like nitric oxide, 5-hydrooxytryptamine, coagulating factors, C-reactive protein (CRP), histamine, hypothalamic activity before migraine attack, activation of trigeminovascular (TGV) system,[5] activation of brainstem nucleus, inflammatory biomarkers like PTX-3, calcitonin gene related peptide (CGRP) and many cytokines.[6]

While studying the inflammatory aspect of migraine, many nociceptors are stimulated by the inflammatory mediators released by damaged endothelium and then activate trigeminovascular pathway which in return sensitize various brain areas. Pentraxin-3 is a long chain pentraxin and release from vascular endothelial cells in reaction to inflammatory processes.[7,8] It is considered as a novel biomarker for diagnostic purposes in migraine patients and other inflammatory diseases.[9] Pentraxin-3 also serve as a chemo-attractant in complement system activation and have a role in immune reactions. Many studies described the strong associations of pentraxin-3 in inflammatory conditions.[10] As we want to evaluate the inflammatory aspect of migraine, the aim of our study was to investigate the levels of pentraxin-3 in migraine patients without aura and in healthy controls.

## METHODS

This study was designed as a cross-sectional comparative study. The study was done at the department of IMBB Physiology, University Of Lahore, Lahore Pakistan. Sample size was calculated to be 1 per group using the formula of means [$n=\sigma 2(Z1-\alpha+Z1-\beta)/(\mu o-\mu a)2$] and by the study of dominguez at el. We took 80 samples for the better power of the study and consumption of purchased kits (Elabscience Human PTX3/TSG-14 (pentraxin 3) ELISA kit).

We took 40 diagnosed migraine patients and 40 healthy controls. Migraine was diagnosed on the criteria of international headache disorders beta version. Written informed concent was obtained by each of them. A proforma was filled up by patients and controls. To exclude hypertention and diabetes, blood pressure and blood glucose levels were measured. 5ml blood sample was taken from antecubital vein by each participant and centrifuged for 15minutes to obtain serum and then stored in ependroff vials at -200°C for further use in ELISA. Ptx-3 levels in pg/ml were obtained by ELISA.

We included participants from all age groups, took patients of migraine without aura, healthy controls, no other acute or chronic ailment in both cases and controls, BMI was calculated by weight in kg /height in $m^2$. We excluded all other inflammatory diseases. SPSS version 22 was used for statistical analysis. Shapiro wilk test was used for normality of data which was reported to be non-normal as the p value was $<0.05$. Continuous variables are expressed in means and categorical in frequency(%). Mann–Whitney U test is used to obtain comparison of serum ptx3 in patients and controls. P value $\leq 0.05$ was considered significant.

## RESULTS

All age ranges and both genders were represented within the research participants. Each participant was of Pakistani Punjabi background. The average age of migraine patients was 26±7.78years, while the average age of controls was 25±6.06 years. The control group (n = 40) consisted of healthy individuals without any chronic illness, whereas the case group (n=40) consisted of migrainers with aura but no other chronic condition. The cases had a higher PTX3 levels than the control groups. The mean pentraxin 3 levels in patients with a diagnosis of migraine headache were 145.75±57.7 pg/l, while the levels in controls were 43.65±33.01

pg/L.

Frequency of female patients was more and average BMI was in category 18 to 25. Table 1 illustrates the detailed data. Sign and symptoms varied in each patient, 95% of our recruited patients complained about photobhobia, 75% complained about phonophobia, 72 0.5% suffered from nausea, 42.5 % complained vomiting and 25% of them had atypical abdominal dyscomfort. (Figure 1)

***Table 1:*** *Frequency Distribution of Demographic Parameters with Migraine & without Migrain (n=80)*

| Demographic Categories | with Migraine (n=40) (%) | without Migraine (n=40) (%) |
|---|---|---|
| **GENDER** | | |
| Male | 17 (42%) | 22 (55%) |
| Female | 23 (58%) | 18 (18%) |
| **MARITAL STATUS** | | |
| Yes | 16 (40%) | 14 (35%) |
| No | 24 (60%) | 26 (65%) |
| **BMI** | | |
| <18 | 10 (25%) | 10 (25%) |
| 18-25 | 24 (60%) | 20 (50%) |
| >25 | 6 (15%) | 10 (25%) |
| **SMOKING STATUS** | | |
| Yes | 3 (7.5%) | 8 (20%) |
| No | 37 (92%) | 32 (80%) |
| **USE OF PROPHYLACTIC DRUG** | | |
| Yes | 5 (12.5%) | 0 (0%) |
| No | 35 | 40 (100%) |

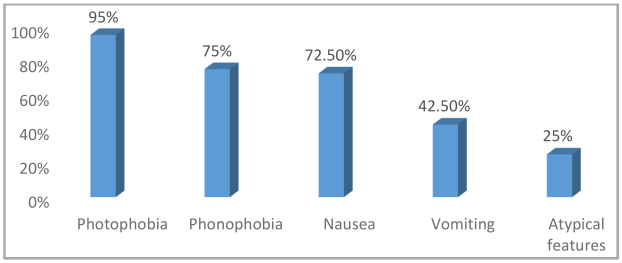


**Figure 1:** Signs and Symptoms of migraine headache

Most of the patients complained that stress, intense lights and skipping meals are major triggering factors in migraine attack. Other factors are sleep disturbance, weather changes, loud noises, traveling, specific food, strong odours and fluctuation in hormones are mentioned in given figure 2.

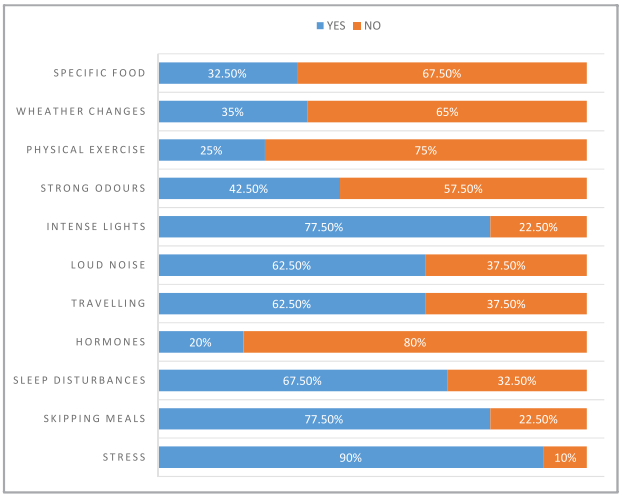


**Figure 2:** *Triggering factors*

Using the Mann-Whitney U test, the serum pentraxin-3 levels in patients and controls were compared. In migraine patients the median (IQR) was computed as 100.55 (84) while in the control group, it was 31.15 (38.8). P-value 0.0001 indicate that it is significant.

***Table 2:*** *Comparison of PTX-3 in cases and controls.*

| Category | Median (IQR) (pg/l) | P-value |
|---|---|---|
| Cases (n=40) | 100.5 (84) | 0.0001* |
| Controls (n=40) | 31.15 (38.8) | |

**p value <0.05 is considered significant*

## DISCUSSION

Migraine is regarded as an inflammatory disease. Trigeminovascular system and other brain areas are sensitized in response to inflammatory mediators. We studied that the biomarker PTX-3 is increased in the migraine patients without aura when compared with control group. PTX3 that have a role in inflammatory diseases and endothelial dysfunction, it is notified to be a novel biomarker in migraine headache pathophysiology.[11]

Ceylan et al. study described that biomarker PTX-3 levels were raised in acute migraine patients and decreased in chronic migraine patients.[8] It was due to the fact that the inflammatory reactions and release of PTX-3 was raised initially and can cause migraine but chronicity of disease causes reduced inflammatory processes and decreased release of PTX-3 were observed. Our study coincides with this, as most of our patients

were mostly diagnosed with acute migraine and raised PTX-3 levels were noticed in serum of migraine patients without aura. Pentraxin-3 is an inflammatory biomarker and role of inflammation in migraine attack generation is well studied. Yavuz et al. studied different paramerters of inflammation in migraine patients and found that fibrinogen, D-dimer, Galactin-3 levels were raised in migraine patients as compare to control group.[12] Raised serum pentraxin-3 levels were also observed in the patients of stroke, myocardial infarction, multiple seclerosis, arthritis, and other inflammatory disease conditions in the previous studies.[13,14]

Role of different parameters like stress, hormonal imbalance, BMI, marital status, and smoking in generation of migraine were observed. The frequency of female suffering from migraine was more compared to men. Other studies also described that young females and reproductive hormones may have a role in migraine headache.[15] Most of the migraine patients in our study were not obese which is contrary to this Ornelo at al. studied that increased BMI have a significant role in migraine attack generation.[16] We included all age groups in our study. Also we observed from the previous study that raised pentraxin-3 may also happen in pediatric migraine.[17]

There are several limitations to our study i.e. short sample size, subjective criteria for diagnosing migraine, and obtain pentraxin-3 value by single serum sample of each participant.

One of the major limitation of our study was that the criteria used to diagnose migraine was subjective. Two other limitations were the limited number of regions covered and the small number of participants. Another significant limitation was that each patient who was diagnosed with migraine had their PTX-3 level measured using a single blood sample.

## CONCLUSION

Serum pentraxin-3 levels are significantly raised in migraine patients without aura and different parameters have a role in migraine.

**Ethical Approval:**

The ethical Approval was obtained from University of Lahore.

**Conflict of Interest:** *None*

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