

## Relation of migraine headache with gastro-intestinal disorders

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### ABSTRACT

An observational study was designed to study the relation of migraine headache with gastro-intestinal disorders. 2948 cases of Migraine clinically diagnosed by Ayush doctors working at various Institutions under the purview of Directorate of Ayush, Jammu & Kashmir, India were enrolled in the study. The data of the patients was recorded in Case Record Forms and a questionnaire specially designed for the purpose. The study reveals that the Gastro-intestinal disorders along with co-relation of various Intestinal Gases play a major role in triggering the episodes of migraine attacks.

**Key words:** Migraine, Headache, Gastrointestinal disorders, Ayush

Headache is among the most common reasons patients seek medical attention, on a global basis being responsible for more disability than any other neurologic problem. Diagnosis and management are based on a careful clinical approach augmented by an understanding of the anatomy, physiology, and pharmacology of the nervous system pathways mediating the various headache syndromes. A classification system developed by the International Headache Society characterizes headaches as primary or secondary (Table 1). Primary headaches are those in which headache and its associated features are the disorder itself, whereas secondary headaches are those caused by exogenous disorders. Primary headache often results in considerable disability and a decrease in the patient's quality of life. Mild secondary headache, such as that seen in association with upper respiratory tract infections, is common but rarely worrisome [1].

Headache is the symptom of pain in the face, head, or neck. It can occur as a migraine, tension-type headache, or cluster headache [2, 3]. Headaches can occur as a result of many conditions. There are a number of different classification systems for headaches. The well-recognized is that of the International Headache Society, which classifies it into more than 150 types of primary and

secondary headaches. Causes of headaches may include dehydration; fatigue; sleep deprivation; stress [4]. The effects of medications (overuse) and recreational drugs, including withdrawal; viral infections; loud noises; head injury; rapid ingestion of a very cold food or beverage; and dental or sinus issues [5,6].

There are so many cases of headache that dedicated headache clinics have been established in many medical centers. In addition to its frequency in general practice, many headaches are caused by medical rather than neurologic diseases and the subject is the legitimate concern of the general physician. Yet there is always the question of intracranial disease so that it is difficult to approach the subject without knowledge of neurology. Why so many pains are centered in the head is a question of some interest. Several explanations come to mind. For one thing, the face and scalp are more richly supplied with pain receptors than

**Table 1: Classification of Headaches**

Primary Headache Type	%	Secondary Headache Type	%
Tension-type	69%	Systemic infection	63%
Migraine	16%	Head injury	4%
Idiopathic stabbing	2%	Vascular disorders	1%
Exertional	1%	Subarachnoid hemorrhage	<1%
Cluster	0.1%	Brain tumor	0.1%

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### Access this article online

Received – 06<sup>th</sup> June 2023

Initial Review – 26<sup>th</sup> June 2023

Accepted – 22<sup>nd</sup> July 2023



Quick Response Code

many other parts of the body, perhaps to protect the precious contents of the skull. Also, the nasal and oral passages, the eye, and the ear—all delicate and highly sensitive structures—reside here and must be protected; when

affected by disease, each is capable of inducing pain in its own way. Finally, there is great concern by patients about what happens to the head perhaps more than other parts of the body because headache raises the specter of brain tumor or other cerebral disease [6,7]

**Table 2: Differential diagnosis of headaches [6]**

Tension headache	New daily persistent headache	Cluster headache	Migraine
Mild to moderate dull or aching pain		Severe pain	Moderate to severe pain
Duration of 30 minutes to several hours	Duration of at least four hours daily Occur In Periods Of 15 Days A Month for Three Months	Duration of 30 minutes to 3 hours May Happen Multiple Times in A Day for Months	Duration of 4 hours to 3 days Periodic Occurrence; Several Per Month to Several Per Year
Located as tightness or pressure across head	Located on one or both sides of the head Consistent Pain	Located one side of head focused at eye or temple Pain Describable as Sharp Or stabbing	Located on one or both sides of head Pulsating Or Throbbing Pain
No nausea or vomiting			Nausea, perhaps with vomiting
No aura	No aura		Auras
Uncommonly, light sensitivity or noise sensitivity		May be accompanied by running nose, tears, and drooping eyelid, often only on one side	Sensitivity to movement, light, and noise
	Exacerbated By Regular Use Of Acetaminophen Or NSAIDS		May Exist with Tension Headache [6].

Migraine the second most common cause of the headache and the most common cause of headache related and induced neurologic cause and disability in the world afflicts 15% of women and 6% of men over a one-year period. The sensory sensitivity that is characteristic of migraine is probably due to dysfunction of monoaminergic sensory control systems located in the brain stem and hypothalamus. Pharmacological and other data point to the involvement of neurotransmitter 5-Hydroxytryptamine (5-HT, also known as serotonin) in migraine. Common Migraine is the most frequently encountered type of attack. Neurologic accompaniments are inconspicuous. Some people exhibit prodrome a day before the onset of attack, exhibit behavioral changes, depression etc. The prodrome clears as the headache begins but the headache is often accompanied by other vaguely neurologic symptoms such as anorexia, nausea, vomiting, hypersensitivity to noise and light, dizziness etc. Although the word migraine derives from “hemicrania” a one-sided head pain, it is common for the migraine to be bilateral [8].

### Pathophysiology

The cause of migraine is unknown but there is increasing evidence that the aura is due to dysfunction of

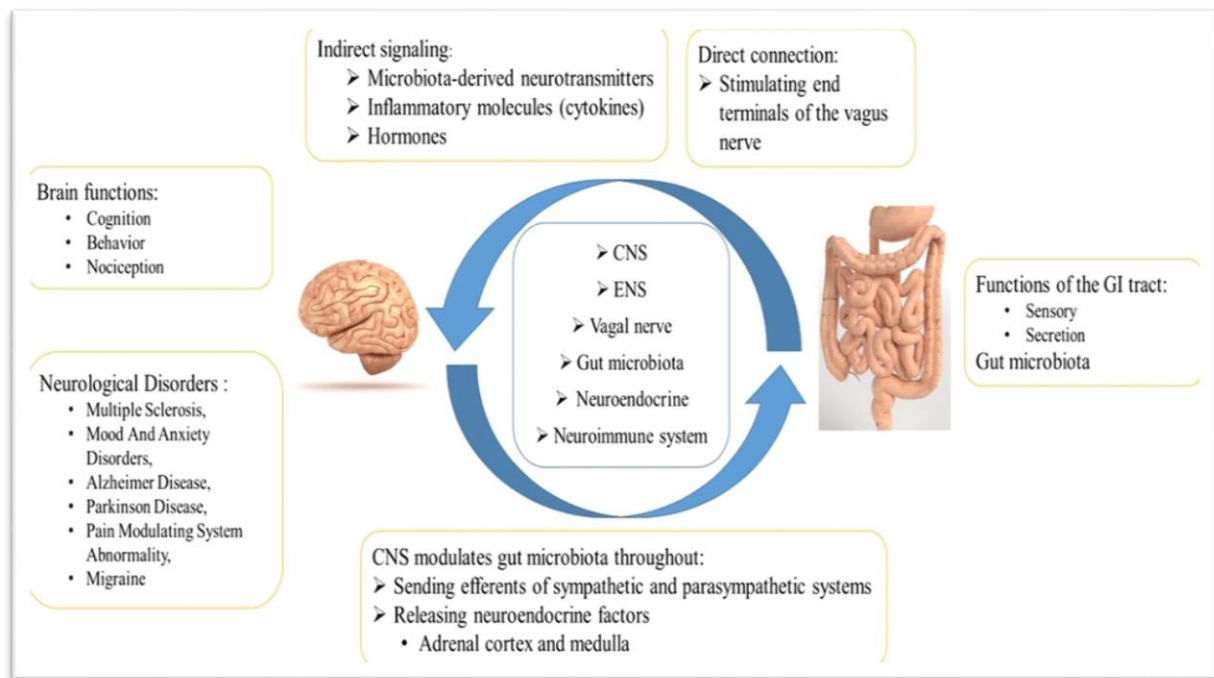
ion channels causing a spreading front of cortical depolarization (excitation), followed by hyperpolarization (depression of activity). The headache phase is associated with vasodilation of extracranial vessels and may be relayed by hypothalamic activity. The female preponderance and the frequency of migraine attacks at certain points in the menstrual cycle also suggest hormonal influences [9]. Currently, most specialists think migraines are due to a primary problem with the nerves in the brain [10]. Auras are thought to be caused by a wave of increased activity of neurons in the cerebral cortex known as cortical spreading depression [11]. Followed by a period of depressed activity [12]. Some people think headaches are caused by the activation of sensory nerves which release peptides or serotonin, causing inflammation in arteries, dura and meninges and also cause some vasodilation. Triptans, medications that treat migraines, block serotonin receptors and constrict blood vessels [13].

### Gastro-Intestinal Disorders in Migraine related Headaches

The terminology “gut-brain axis” points out a bidirectional relationship between the GI system and the central nervous

system (CNS). Brain normally regulates movements and functions of the GI tract (sensory and secretion). Hormonal factors through the hypothalamic pituitary adrenal (HPA) axis by mediating stress responses impact on the gut functions. On the other hand, GI system is believed to be able to affect the CNS. A number of the brain functions such as cognition, behavior and even nociception are under the influence of the gut system. The dysfunction of the gut-brain axis has been implicated in a number of neurological

disorders such as multiple sclerosis, mood and anxiety disorders, Alzheimer disease, Parkinson disease, and migraine [14,15]. Figure 1 depicts the mechanisms of the bidirectional relationship between the gut and the brain in migraine. Several neurotransmitters have been supposed to play a role in this process including serotonin, dopamine, gamma-aminobutyric acid, and calcitonin gene-related peptide (CGRP) [16,17].



**Figure 1: Bidirectional relationship between the gut and the brain in migraine**

The meta-analysis of 5 case-control studies, revealed about 45% of migraineurs harbor *Helicobacter pylori*, while the prevalence rate among healthy controls was estimated at about 33%. It is noteworthy that when aiming at investigating the role of *Helicobacter pylori* infection in headache pathogenesis, various strains of the bacterium, ethnicity of the studied patients, the variation of *Helicobacter pylori* in different regions, and the potential pathological differences which would be present in different subtypes of headache, should be considered [18]. Celiac disease (CD) is an autoimmune multisystem condition caused by gluten peptide in genetically susceptible individuals [19]. According to the available data, the prevalence of CD is 1.4% [20]. A variety of neurologic manifestations have been observed with CD such as epilepsy, ataxia, cerebellar ataxia, mood disorders, encephalitis, peripheral neuropathy, neuromuscular disorders, dementia, learning disorders, developmental delay and migraine [21].

A “nutritional-microbial-epithelial -neuronal” akin to “environmental-luminal-mucosal-neuronal” brain network

may be responsible for these extra-intestinal manifestations [22]. Studies have shown that patients with CD have higher prevalence of migraine compared with healthy controls and vice versa [23,24]. Irritable Bowel Syndrome and migraine share some similarities, i.e., both disorders are chronic, recurrent and more prevalent among women, have high individual/social burden, highly affect the patients’ quality of life, and seem to be accompanied by a number of comorbid psychological diseases especially anxiety. Furthermore, central, visceral and thermal cutaneous hypersensitization are common among both disorders. Overall, 60% of migraineurs have allodynia and IBS patients reported to have allodynia aside from visceral hypersensitivity. N-methyl-D-aspartate (NMDA) may probably be responsible for allodynia among the IBS patients [25].

There is an established association between migraine and IBS, such that IBS was revealed to be common among migraineurs and migraine was reported to be prevalent among IBS suffers [26]. A prevalence cohort study showed that in comparison to non-IBS subjects, IBS patients had a

40–80% higher prevalence odds of migraine, depression, and fibromyalgia [27]. It has been proposed that tryptophan-kynurenine pathway might be one of the main ways by which GI microbiota may affect the function of the CNS due to the presence of synthetic enzymes in bacterial strains of the intestine that may produce tryptophan metabolites (such as quinolinic and kynurenic acids). As tryptophan is the precursor of serotonin, the amount of this neurotransmitter in the brain depends on the levels of this amino acid [28,29].

The role of gut microbiota in anxiety, depression and the HPA axis has been studied through assessing the effects of prebiotics and probiotics administration in these conditions [30,31,32]. Small intestinal bacterial overgrowth (SIBO) is a disorder with no distinct clinical manifestations as it is associated with abdominal pain/discomfort, bloating, flatulence, diarrhea, and constipation that all may be linked to several other syndromes in the gastrointestinal (GI) tract, including irritable bowel syndrome (IBS) Therefore, a precise definition of this disease in the clinical context may lack specificity and consistency. At the cellular level, this disorder is currently defined as occurring with increase in bacterial flora equal to or greater than 10<sup>3</sup> colony-forming units (CFU) per mL, but previously it was postulated even 10<sup>5</sup> CFU/mL of upper gut aspirate [33].

However, we still do not know what bacterial population in the GI tract should be considered as a “normal”. Literature data suggest that such normal population should rather not exceed 10<sup>2</sup> CFU/mL and 10<sup>5</sup> CFU/mL should be attributed to anatomical abnormalities in the GI tract. Tryptophan (Trp) metabolism is involved in the pathogenesis of several gastrointestinal disorders, but little is known on Trp role in SIBO etiology. The SIBO-D patients showed an increased serum concentration of 5-HT and small intestinal mucosa mRNA expression of tryptophan hydroxylase 1 (TPH-1), a rate-limiting enzyme in 5-HT biosynthesis. Urinary 5-hydroxyindoleacetic acid (5-HIAA), the main metabolite of 5-HT, was higher in both group of SIBO patients than controls [34]. As tryptophan is the precursor of serotonin, the amount of this neurotransmitter in the brain depends on the levels of this amino acid [33,34].

### Concept of migraine in Ayurvedic and Unani systems of Medicine (Indigenous Medicines of India)

**Ayurvedic system of Medicine:** Migraine can be correlated to “*Ardhavabhedaka*” in Ayurveda. Detailed description of specific etiology, pathogenesis, and treatment for *Ardhavabhedaka* is explained in treatises. Etiological factors such as excessive consumption of dry substances,

exposure to cold, inappropriate sexual activity, withholding of natural urges, exhaustion, and exercise are quoted as the causes for *Vata* (biological humour ~ neurological function) vitiation. Frequent intake of food before the digestion of a previous meal, intake of heavy to digest food, drinking excess cold water contribute to *Kapha* (biological humour ~ systemic integrity) vitiation and formation of ama (a by-product of impaired metabolism). Due to the above etiological factors, *Vata* alone or along with *Kapha* affects the head and produces severe unilateral pain in the neck, eyebrow, temples, ear, eye, and forehead [35,36].

The treatment in Ayurveda includes *Snehapana* (internal Oleation), *Svedana* (sudation), *Virechana* (Therapeutic Purgation), and *Nasya* (Nasal Instillations), followed by oral intake of Polyherbal and Herbo-mineral medications. Further symptoms of migraine often correlate with those of ‘*Amlapitta*’ (state of hyperacidity) characterized by giddiness, fainting, dysgeusia, fatigue, nausea, vomiting, and headache. Hence, therapies that aid in hyperacidity and correction of digestive fire also aid in improving migraine symptoms. A judicious protocol based on five Ayurvedic medicines can markedly reduce the migraine frequency in some migraine patients. The treatment protocol was derived from the Ayurvedic concept of diagnosis of *Amla-Pitta* a state of acid-alkali imbalance causing one of the symptoms of *Shiro ruja* (headache).

The hypothesis is quite similar to Tissot's idea on the pathogenesis of migraine, viz. that it usually arose from stomach disturbance. Incidentally, there is a close correlation between the symptoms of migraine with those of *Amla-pitta* (state of acid-alkali imbalance in the body) causing symptoms such as: *brahma* (confusion), *moorcha* (fainting), *aruchi* (anorexia), *aalasya* (fatigue), *chardi* (vomiting), *prasek* (nausea), *mukhmadhurya* (sweetness in the mouth) and *shiroruja* (headache). The correlation between the cause and symptoms of *Amla-pitta* match the diagnosis criteria of migraine [37]. Intervention from the level of etiology, pathogenesis, aggravating and relieving factors, and disease-specific management along with diet and lifestyle is vital in Ayurveda. Bio-purificatory measures like *Virechana* and *Nasya* have shown good efficacy as standalone and as an add-on with oral herbal and Herbo-mineral preparations [38].

**Unani System of Medicine:** The word *Shaqeeqa* is derived from an Arabic word ‘shiq’ which means ‘a part’ or ‘a side’. In this disease pain occurs in a part rather than entire head giving it name shaqeeqa [39]. As per classical literature it is a type of *Suda*, in which pain occurs in one side of head and characterized by recurrent episodes that are moderate to severe. If quantity of morbid material is less than this pain



mainly occurs in that part of head which is weak, as it is unable to produce pain in entire head. *Ibn e Sina (Avicenna)* has mentioned that this pain occurs only in a part of head and termed it as *Adha sisi ka dard*. *Galen* describes that this pain is flitting in nature but actually it remains in centre of head and weaker side accepts this pain [40].

A headache described in the Unani medical textbooks namely *Suda e Reehi wa Asabi* in which the cause has been described as the gases which travel to the brain area and cause severe headache. One more type of Headache as *Suda e Medi Balgami* in which the cause has been described as gastric disorders which accompany nausea, vomiting and dyspepsia. Constipation and flatulence have been described as one of the main causes of *Shaqqeqa* (migraine) and is explained on the basis that the harmful gases produced in the body penetrate the brain causing one sided headache, tinnitus and photophobia [41]. Akbar Arzani said that there are two possible causes of *Shaqqeqa*.

- First is that the *Bukharat* (gases) from the whole body or from any organ ascends to the head and accumulates into the weaker side of head and resulting in the form of headache.
- Second is that the morbid humors in arteries accumulate to one side of head and produces pain [42,43].

The treatment protocol in Unani also stresses on the correction of Gastro-intestinal problems and change in lifestyle and diet which includes purgation, bloodletting and avoiding *nafakh* (Faltulent) diets [44].

## METHODOLOGY

**Sample Size:** 2948 Patients (1920 females and 1028 males) who were suffering from Migraine related Headaches.

After taking proper consent from the patients who have been suffering from episodic headaches, they were provided a Questionnaire wherein they were asked relevant questions regarding the present study. Following information was sought from the patients:

1. Location of the Headache (whether parietal, Frontal, Occipital or whole head)
2. Other Symptoms Associated with Headache.
3. Any Gastro-Intestinal Symptoms.
4. Any Relation of Diet with episodes of Migraine.
5. Foods that trigger the episodes of Migraine.
6. Socio-economic Status.

The data of the patients was collected from various Ayush Institutions of Jammu and Kashmir working under

the purview of Directorate of Ayush, Health Department of Jammu & Kashmir. The data was analysed as per the Questionnaire to ascertain if there is any relation between gastro-intestinal disorders with the episodes of Migraine attacks. Accordingly the relation with any particular food, Socio-economic status of the patients was also analysed so that other factors associated with migraine headaches are also established. Only the data of those patients were added in the sample size who consented to be part of this observational study. The data collection was completed in nine months from May 2022 to January 2023. The analysis of the data was done which are mentioned in the below tables (3-8) and accordingly results (inferences) were drawn from the data.

## RESULTS

After analysing the data as per the information from Table 3-8 following observations were made:

1. 2933 Patients out of the total sample size of 2948 patients that is 99% of the patients suffered from one or more associated symptoms of Nausea, Vomiting, Photophobia which are peculiar to Migraine related Headaches. Nausea dominated the symptoms with 90% patients having this symptom.
2. The relation with food was also significant with Lentils, spicy & oily foods and Chocolates leading the chart as the most common food items identified by the patients which triggered the migraine episode.
3. Among the Gastro-intestinal disorders majority of the patients were suffering from bloating (flatulence), Irritable Bowel Syndrome and constipation. Dyspepsia, indigestion and acidity complaints were present in 90% of patients.
4. The females suffered more migraine headaches than males in the ratio of 2:1.
5. The Higher and middle socio-economic class was more affected with migraine related disorders while in lower and below poverty line the disease was less prevalent.
6. Majority of the patients had one sided headache with throbbing pain extending to eyes and neck. Photophobia was not the dominant symptom in majority of the patients.

**Table 3 - Location of the Headache**

Part of Head	Number of Patients
Parietal part	2152
Frontal part	326
Occipital part	238
Whole Head	232
Total	2948

**Table 4: Other Symptoms Associated with Headache**

Symptoms	Number of Patients
Nausea (only)	2047
Nausea/Vomiting (Both)	722
Photophobia	164
No other symptoms	15
Total	2948

**Table 5: Gastro-intestinal symptoms in patients experiencing episodes of migraine headache**

Prevalent Gastro-Intestinal Disorder	Number of Patients
Constipation	897
Flatulence	1078
Dyspepsia	342
Liver Disorders	87
Irritable Bowel Syndrome	544

**Table 6: Relation of Diet with the Episodes of Migraine Headaches**

Food Habits	Number of Patients
Vegetarian	665
Mixed	2283
Total	2948

**Table 7: Foods that Trigger Migraine Headache**

Food	Number of Patients
Cheese	351
Peas/Rajma (Lentils)	751
Chocolates	444
Fast Food	667
Mutton	257
Chicken	11
Fish	10
Spicy food	741
Oily/fatty foods	654

**Table 8: Socio economic status of patients experiencing migraine headaches**

Socio Economic Status	Number of Patients
Upper Class	1156
Middle Class	1286
Lower Middle Class	255
Lower Class (BPL)	251
Total	2948

## DISCUSSION

The observations made in the patients suffering from migraine attacks clearly reveal the following:

1. There are Gastro-intestinal factors associated with the migraine attacks.
2. Diet also plays a significant role in triggering the episodes.
3. The stress levels in patients suffering from migraine headaches is higher and majority of these patients also suffer from other stress related disorders e.g IBS and Anxiety neurosis.
4. The socio-economic condition of the patients also played a role. It has been seen that Upper and Middle-class people commonly live a sedentary life style and have more anxiety related disorders. The lower economic class people commonly are hardworking with majority being the labour class wherein prevalent headache observed was due to some secondary cause viz a viz febrile conditions or infectious diseases of the brain.
5. The Gastro-intestinal disorders do play major role in triggering the episodes of migraine attacks. It is observed that the exaggerating factors along with the gastro-intestinal disorders are stress, diet and lifestyle.

If we carefully study the complaint of the 90% patients what they described in their own way was that complained that it looks like that some harmful gases travel from the GI tract to the head and trigger the headache. This type of symptom can only be recorded by a medical professional in a health institution with no support from any modern medical literature. The same patho-physiology has been described in the Ayurvedic and Unani textbooks besides the treatment protocols established as per this patho-physiology in these systems has provided efficient results in the patients suffering from migraine.

Now, if there definitely is an axis between Gastro-intestinal disorders and migraine headaches what is the causative factor in the GI tract which triggers the chemical reaction in the brain and causes episodic migraine headaches? As discussed there is a pre-biotic relation for migraine headaches. Hydrogen (H<sub>2</sub>) and methane (CH<sub>4</sub>) are mostly produced in the large intestine of normal subjects, during the partial or full fermentation of the undigested polysaccharide fraction of certain carbohydrates by the anaerobic flora. The methane gas produced in the intestines was previously been considered an inactive gas that it is mainly excreted in flatus, while a certain amount is excreted in breath [45].

However, recently, methane has been associated with gastrointestinal disorders, mainly chronic constipation and constipation predominant irritable bowel syndrome (IBS), as well as metabolic diseases like obesity [45,46]. The study by Triantafyllou K, Chang C, Pimentel M. titled

“Methanogens, methane and gastrointestinal motility” conducted in 2014 establishes role of methane in IBS and chronic constipation. The study in its conclusion refers to Methane is a unique gas produced in strict anaerobic conditions by intestinal methanogens that metabolize H<sub>2</sub>, one of the end products of bacterial fermentation. Although thought of as an inert gas, there is evidence from translational medicine that methane acts like a neuromuscular transmitter resulting in reduced propagation of the peristaltic movement in the intestine. This evidence is further supported by the universal finding in physiological studies that CH<sub>4</sub> production (measured by breath testing) delays transit time and by clinical studies showing a relationship between methane statuses on breathe testing with delayed transit associated conditions like constipation predominant IBS and chronic constipation [47].

There is a decreased level of neurotransmitter, serotonin in migraineurs [48]. Migraine is painful recurrence of headache due to variation in the blood flow of cerebral blood vessels. This is caused by activation of ‘trigemino vascular system’, which causes release of vasodilators e.g. calcitonin gene-related peptide (CGRP) and diminution of the levels of neurotransmitter like serotonin in trigeminal nerve and cranial vessels [48]. So it becomes established that migraine patients have decreased level of serotonin which triggers the activation of Trigemino vascular system and causes severe vasodilatation. The intestinal gas which decreases the serotonin levels is methane (CH<sub>4</sub>) which is established by the study titled “IBS subjects with methane on lactulose breath test have lower postprandial serotonin levels than subjects with hydrogen” conducted by Mark Pimentel, Yuthana Kong & Sandy Park and published in Digestive Diseases and Sciences volume 49, pages 84–87 (2004) wherein it was concluded that “The postprandial serotonin level in methane producing IBS subjects was lower than in hydrogen producers.

Methane producers had a reduction in serotonin after glucose. Methane producing IBS subjects have reduced postprandial serotonin. Whether methane is a surrogate marker of constipation or contributing to the reduced serotonin remains to be determined [49]. Serotonin is a neurotransmitter which, among many functions, participates in peristaltic control of the gut. In fact, the majority of serotonin in the human body is found in the gastrointestinal tract. Halogenated methane is able to inhibit the pulmonary uptake of serotonin in rat lung [50]. Although it has been shown that aberrations exist in both CH<sub>4</sub> and serotonin in IBS, it is still unclear whether these two molecules work together to influence gut motor function [51].

## CONCLUSION

The results of the present study establishes that there certainly exists a relation of migraine headache with gastro-intestinal disorders whether it is bloating, IBS, Dyspepsia or all of these. The pathophysiology documented before hundreds of years for migraine in Ayurvedic and Unani system of medicine also suggests a broader axis between migraine and gastro-intestinal disorders. The fact is established through the treatment protocols of migraine followed in Ayurvedic and Unani systems of medicine in which the main stress is given to treating the gastro-intestinal disorders and time has proven that these treatment methods have provided relief to the patients suffering from migraine. The connection with any particular food items which trigger the episodes of migraine has also been established where we observed that lentils and spicy foods trigger episodes of migraine attacks in some patients.

Patients suffering from flatulence, constipation, IBS have been observed to have high chances of migraine attacks. The gases produced in the gut seem to play a role in exaggerating the migraine attacks particularly methane gas (CH<sub>4</sub>) which is the only gas produced in the intestines having a role in reducing the serotonin levels and is very well observed in migraine. Further studies are needed where patients having episodes of migraine may be subjected to breath testing for evaluation of methane concentration in the blood and then according to the results further researches be undertaken. Stress and life style are two other important factors which have been observed to exaggerate the migraine attacks in this study. Further evaluation with clinical trials is needed to further establish the findings.

## REFERENCES

1. Jameson, Fauci, Kasper, et al. Harrison's Principles of Internal Medicine V-2; Chapter 422; P 3096; Migraine and other primary headache disorders.
2. "Headache disorders". The World Health Organization. 8 April 2016. Retrieved 2021-12-14.
3. Silberstein, Stephen D. (2022-03-09), Lynch, Mary E.; Craig, Kenneth D.; Peng, Philip W. (Eds.), "Headache", *Clinical Pain Management* (1 ed.), Wiley, pp. 336–342,
4. Britton, Carolyn B, Green, et al. (Eds.), "Stress and headache", *The Neuropsychiatry of Headache*, Cambridge: Cambridge University Press.2013;54–62,
5. "Headache Causes". Mayo Clinic. Retrieved 21 October 2019.
6. Smetana GW "Chapter 9. Headache". In Henderson MC, Tierney Jr LM, Smetana GW (Eds.). *The Patient History: An Evidence-Based Approach to Differential Diagnosis*. New York, NY: McGraw-Hill. Archived from the original. 2015
7. Allan H. Ropper, Martin A. Samuels, Joshua P. Klein, Sashank Prasad Adams and Victor's Principles of Neurology, 11<sup>th</sup> edition

8. Jay H Stein, Internal Medicine Volume II, Third Edition Chapter 288 Headache and Facial Pain; page 1917
9. Stuart H. Ralston, Ian D. Penman, Mark W.J Strachan, et al. Davidson's Principles and Practices of Medicine; 23<sup>rd</sup> edition; Chapter Neurology; Headache syndromes Page 1095.
10. Cutrer FM, Bajwa A, Sabhat M. Post TW (Eds). "Pathophysiology, clinical manifestations and diagnosis of migraine in adults". Up To Date. San Francisco, CA: Walters Kluwer. Retrieved 23 April 2014.
11. Hadjikhani N, Sanchez Del Rio M, Wu O, et al. "Mechanisms of migraine aura revealed by functional MRI in human visual cortex". Proceedings of the National Academy of Sciences of the United States of America. 2001;98 (8): 4687–4692.
12. Buzzi MG, Moskowitz MA. "The pathophysiology of migraine: year 2005". The Journal of Headache and Pain. 2005;6 (3): 105–111.
13. Denny CJ, Schull MJ. "Chapter 159. Headache and Facial Pain.". In Tintinalli JE, Stapczynski J, Ma O, Cline DM, Cydulka RK, Meckler GD (eds.). Tintinalli's Emergency Medicine: A Comprehensive Study Guide (7th ed.). New York, NY: The McGraw-Hill Companies 2011.
14. Mayer EA, Tillisch K, Gupta A. Gut/brain axis and the microbiota. J Clin Invest. 2015;125(3):926–938
15. Hindiyeh N, Aurora SK. What the gut can teach us about migraine. Curr Pain Headache Rep.2015; 19(7):33
16. Asano Y, Hiramoto T, Nishino R, et al. Critical role of gut microbiota in the production of biologically active, free catecholamines in the gut lumen of mice. Am J Physiol Gastrointest Liver Physiol. 2012;303(11):G1288–G1295
17. Barrett E, Ross RP, O'Toole PW, et al. Gamma-Aminobutyric acid production by culturable bacteria from the human intestine. J Appl Microbiol.2012; 113(2):411–417
18. Camara-Lemarroy CR, Rodriguez-Gutierrez R, Monreal-Robles R, et al. Gastrointestinal disorders associated with migraine: a comprehensive review. World J Gastroenterol.2016;22(36):8149–8160
19. Shannahan S, Leffler DA. Diagnosis and updates in celiac disease. Gastrointest Endosc Clin N Am.2017; 27(1):79–92
20. Singh P, Arora A, Strand TA, et al. Global prevalence of celiac disease: systematic review and meta-analysis. Clin Gastroenterol Hepatol.2018;16(6):823–836 e2
21. Rani U, Imdad A, Beg M. Rare neurological manifestation of celiac disease. Case Rep Gastroenterol .2015;9(2):200–205
22. Aaron L, Torsten M, Patricia W. Autoimmunity in celiac disease: Extra-intestinal manifestations. Autoimmun Rev. 2019;18(3):241–246
23. Zis P, Julian T, Hadjivassiliou M. Headache associated with coeliac disease: a systematic review and meta-analysis. Nutrients. 2018;10(10):144
24. Dimitrova AK, Ungaro RC, Lebwohl B, et al. Prevalence of migraine in patients with celiac disease and inflammatory bowel disease. Headache. 2013;53(2):344–355
25. Arzani M, Jahromi S.R, Ghorbani Z. Gut-brain Axis and migraine headache: a comprehensive review. J Headache Pain 21, 15 (2020).
26. Camara-Lemarroy CR, Rodriguez-Gutierrez R, Monreal-Robles R, et al. Gastrointestinal disorders associated with migraine: a comprehensive review. World J Gastroenterol .2016;22(36):8149–8160
27. Cole JA, Rothman KJ, Cabral HJ, et al. Migraine, fibromyalgia, and depression among people with IBS: a prevalence study. BMC Gastroenterol.2006; 6(1):26
28. Maqsood R, Stone TW. The gut-brain Axis, BDNF, NMDA and CNS Disorders Neurochem Res .2016;41(11):2819–2835
29. Clarke G, Grenham S, Scully P, et al. The microbiome-gut-brain axis during early life regulates the hippocampal serotonergic system in a sex-dependent manner. Mol Psychiatry.2013;18(6):666–673
30. Saulnier DM, Ringel Y, Heyman MB, et al. The intestinal microbiome, probiotics and prebiotics in neurogastroenterology. Gut Microbes.2013;4(1):17–27
31. Foster JA, Neufeld K-AM. Gut–brain axis: how the microbiome influences anxiety and depression. Trends Neurosci.2013;36(5):305–312
32. Ghorbani Z, Nazari S, Etesam F, et al. The effect of Synbiotic as an adjuvant therapy to fluoxetine in moderate depression: a randomized multicenter trial. Arch Neurosci .2018;5(2):e60507
33. Khoshini R, Dai S.C, Lezcano S, et al. A systematic review of diagnostic tests for small intestinal bacterial overgrowth. Dig. Dis. Sci. 2008;53:1443–1454.
34. Chojnacki C, Popławski T, Konrad P, et al. Serotonin Pathway of Tryptophan Metabolism in Small Intestinal Bacterial Overgrowth-A Pilot Study with Patients Diagnosed with Lactulose Hydrogen Breath Test and Treated with Rifaximin. J Clin Med. 2021;10(10):2065.
35. Trikamji VY, Charaka C. Ayurveda Dipika Commentary, Charaka Samhitha. Vol. Siddhithana 9/74. Varanasi: Chaukhambha Surbharati Prakashan; 2013.
36. Vd Paradkar HS, A, Vagbhata. Astanga Hridaya, Sarva-ngasundara commentary. Vol. Uttarasthana 23/7. Varanasi: Chaukhambha Surbharati Prakashan; 2014.
37. Vaidya PB, Vaidya BS, Vaidya SK. Response to Ayurvedic therapy in the treatment of migraine without aura. Int J Ayurveda Res. 2010 Jan;1(1):30-6.
38. Soman A, Venkatram S, Chikkanna U, et al. Ayurveda for management of migraine: A narrative review of clinical evidence. J Family Med Prim Care. 2022 Aug;11(8):4228-4235.
39. Tabri ABM. Moalajat-e-Buqratiya. Vol 1. New Delhi: CCRUM; 1995: 284-290.
40. Riyazuddin M, Shahid A, Nagaraj RB, et al. Migraine (Shaqqeqa) and its management in Unani medicine. Drug Metab Pers Ther. 2021 Aug 13.
41. Waseem A Azmi, Moalijat Vol 1, published by Central Council for promotion of Urdu language; page 42, 48, 72.
42. Arzani HA. Tib e Akbar. (Urdu translation by Hakim Mohammad Hussain). Deoband: Faisal Publications; YNM: 20-21.
43. Majoosi AIA. Kamilussina. (Urdu translation by Ghulam Hussain Kantoori). Vol 2. New Delhi: CCRUM; 2010: 544-545.
44. [https://www.nhp.gov.in/shaqqeqa-migraine\\_mtl](https://www.nhp.gov.in/shaqqeqa-migraine_mtl)
45. Sahakian AB, Jee SR, Pimentel M. Methane and the gastrointestinal tract. Dig Dis Sci. 2010;55:2135–2143.
46. Roccarina D, Lauritano EC, Gabrielli M, et al. The role of methane in intestinal diseases. Am J Gastroenterol. 2010;105:1250–1256.



47. Triantafyllou K, Chang C, Pimentel M. Methanogens, methane and gastrointestinal motility. *J Neurogastroenterol Motil.* 2014 Jan;20(1):31-40.
48. Aggarwal M, Puri V, Puri S. Serotonin and CGRP in migraine. *Ann Neurosci.* 2012 Apr;19(2):88-94.
49. Pimentel M, Kong Y, Park S. IBS subjects with methane on lactulose breath test have lower postprandial serotonin levels than subjects with hydrogen. *Dig Dis Sci.* 2004 Jan;49(1):84
50. Hede AR, Andersson L, Post C. Effect of a homologous series of halogenated methanes on pulmonary uptake of 5-hydroxytryptamine in isolated perfused rat lung. *Acta Pharmacol Toxicol (Copenh).* 1985;57:291-296.
51. Sahakian AB, Jee SR, Pimentel M. Methane and the gastrointestinal tract. *Dig Dis Sci.* 2010 Aug;55(8):2135-43.

**How to cite this article:** Mohan Singh, Wahid ul Hassan, Rakesh K Raina. Relation of migraine headache with gastro-intestinal disorders. *Indian J Integr Med.* 2023; 3(3): 62-70.

*Funding: None;      Conflicts of Interest: None Stated*