

Evaluation of *Helicobacter pylori* infection in patients with common migraine headache

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Abstract

Introduction: Migraine can cause headache in different communities so that 12-15% are suffering worldwide. Recently the relationship between infectious diseases such as *Helicobacter pylori* infection and migraine headache has been the focus of many studies. The current study was designed to evaluate IgG and IgM antibodies to *H. pylori* in patients suffering from migraine headaches.

Material and methods: Patients who had diagnostic criteria for migraine were chosen as cases compared to some healthy individuals as the control group amongst which immunoglobulin G (IgG), immunoglobulin M (IgM), age, job, gastro-intestinal (GI) disorders, history of migraine, special meals, medications, sleeping disorders, stress, environmental factors etc were analysed.

Results: The prevalence of disease was 38.6%. Household women had the highest prevalence (40%). Among them menstruation was related to high prevalence of migraine. 75.6% of patients had gastrointestinal disorders of which the gastric reflux was the most important sign (47.1%). The mean optical density (OD) value of IgG and IgM antibody to *H. pylori* was 60.08 ±7.7 and 32.1 ±8.7 for the case group, 21.82 ±6.2 and 17.6 ±9.4 for the control group, respectively.

Conclusions: There was a significant difference in mean OD value of both antibodies to *H. pylori* amongst the case and control groups. As a result, active *H. pylori* infection is strongly related to the outbreak and severity of migraine headaches, and *H. pylori* treatment reduces migraine headaches significantly. Hopefully, the definite treatment and eradication of this infection can cure or reduce the severity and course of migraine headaches significantly if not totally.

Key words: migraine, *Helicobacter pylori*, antibody titre, headache.

Introduction

Migraine is one of the most common types of headache worldwide, affecting 12-15% of the world population and also the main headache for which patients refer to specialist nerve clinics. The headache can be mild to severe and might have one or all symptoms such as photophobia, throbbing, nausea and vomiting. The pain severity depends on the activity and number of its outbreaks [1-6]. Migraine is divided into 4 categories: migraine with aura (classic migraine), migraine without aura (common), other types of migraine, and cluster headache [5-7]. Different types of migraine have been proposed in most resources including ophthalmological migraine, proximate migraine, migraine with complication, children's

migraine and abdominal migraine [5, 6]. When differential diagnosis of migraine is the case, all types of headaches should be considered, such as acute suppurative sinusitis, glaucoma, bacterial meningitis, subarachnoid haemorrhage, pheochromocytoma, abnormalities of brain vessels, high blood pressure after stress headaches, cluster headaches and brain tumours [5]. The pathogenesis of headache is divided into three phases: the first phase is pain at the back of the brainstem; the second is vasomotor activity causing contraction or expansion of arteries inside and outside the brain; and the third phase is activation of medullar nerve cells of triple core (Caudalis) and consequently neuropeptide release of vasomotor at the end of the triple nerve vessels [5, 6]. It also seems that serotonin has a significant role in the creation of migraine headache. Stimulating serotonergic cells cause migraine headaches, increasing cerebral blood flow, and also reserpine, which is a serotonin evacuator, is considered as a cause of pain in migraine [7, 12].

Many factors such as genetics, food and medications, sleep disorders, stress, environmental factors such as noise, light, different smells and humidity, work-related factors, menstruation, severe trauma, alcohol, etc, have been recognized as facilitating factors and the cause of migraine headaches so far [5]. Recently the role of infectious diseases, the immune responses, and also the impact of digestive system disorders on migraine headaches have been noted.

This is a flagellated bacteria from the *Spirillaceae* family of which 11 serotypes in the stomachs of other mammals are recognized, though only the *H. pylori* type has been seen in humans. Some researchers have studied the role of this bacterium in creating acute and chronic gastritis, and gastrointestinal lesions, adenocarcinoma and lymphoma of the stomach [14].

Due to the fact that this bacterium can cause the secretion of serotonin from platelets, releasing PAF, it can play a role in creating migraine headaches by increased secretion of serotonin. However, new research that started in 2002 focused on the role of *H. pylori* activity in creating migraine headaches. As the prevalence of *H. pylori* infection amongst adults living in developed and developing countries is relatively high (40-50% and 80% respectively) and because there is a high proportion of children infected by *H. pylori*, consequently increasing the prevalence of migraine headaches, the current study was designed to evaluate migraine headaches and their relationship with the antibody titre to *H. pylori* infections.

Material and methods

This is a case-control study analysing 70 patients with definite diagnosis of migraine including 24 men

(33.4%), and 46 women (76.5%), with age ranging from 17 to 52 years referring to private clinics in Ilam. The diagnostic criteria of migraine headache used in the current study were according to the International Headache Society including unilateral pain (affecting one half of the head) and pulsating in nature and lasting from 4 h to 72 h, having some symptoms including nausea, vomiting, photophobia and phonophobia, where the symptoms are aggravated by routine activity.

Also 70 healthy people without any history of migraine were randomly selected as the control group. Required information including age, sex, gastro-intestinal (GI) disorder, job, history of migraine in family, blood groups, diet, degree of headache and sleep disorder was obtained from all the people in the case and control groups by interviewing and completing a questionnaire. The antibody (immunoglobulin G – IgG, immunoglobulin M – IgM) titre of all individuals in the case and control groups against *H. pylori* infection was assessed by Enzyme Linked Immunosorbent Assay (ELISA). Data are expressed as mean values \pm standard deviation (SD). The one-sample Kolmogorov-Smirnov test was used to check the normality assumption of the age, and continuousness of variables. χ^2 test was used to compare nominal and ordinal variables in case and control groups. Values of $p < 0.05$ were considered as significant.

This study was presented to the ethical committee of Ilam University of Medical Sciences and was approved by this committee. Written informed consent was provided by all participants.

Results

The frequency of blood groups A, B, O and AB amongst individuals of case and control groups was 35.7%, 9.9%, 50% and 4.3%, respectively (Tables II, III) while 58.5% were Rh positive. Group O was the most prevalent blood group among patients with migraine. Housewives with the highest prevalence of migraine headaches were in the first place, followed by students in the second and employers in the third place (Table III). About 75.7% of those patients who had migraine suffered from GI

Table I. Comparison of age, IgM and IgG in control and migraine groups

Variables	Healthy control (n = 70) Mean \pm SD	Migraine (n = 70) Mean \pm SD	Value of p
Age [years]	35 \pm 9.6	31.5 \pm 8.1	0.12
IgM	17.6 \pm 9.4	32.1 \pm 8.7	0.03
IgG	21.82 \pm 6.2	60.08 \pm 7.7	0.04

IgM – immunoglobulin M, IgG – immunoglobulin G

Table II. Frequency of each studied variable in migraine group

Variables	Highest frequency	Percent
Blood group (ABO)	Group O	50
Blood group (RH)	+	58.5
Occupation	Household women	40
Literacy	Diploma	30
GI disorders	+	75.5
GI disorder types	Reflux	47.1
History of migraine in family	+	54.3
Cause of headache	Stress	21.4
Origin of headache	Frontal	55.7
Sleep disorder	Insomnia	38.6
Special foods	Cheese	17.1
Impact of stress on migraine	+	71.4
Impact of noise on migraine	+	80
Impact of intense light on migraine	+	51.9
Impact of head trauma on migraine	+	52.9
Impact of menstruation on migraine	+	69.5
Loss of appetite and migraine	+	97.1
Prevalence of anxiety following headache	+	91.4
Eye pain and migraine	+	81.6

Table III. Comparison of job, sex and environmental parameters in control and migraine groups

Parameters	Healthy control (n = 32)	Migraine (n = 38)	Value of p
Job, n (%):			
Household	12 (46.2)	14 (53.8)	0.96
Employee	4 (50)	4 (50)	
Other	16 (44)	20 (55.6)	
Sex:			
Male	9 (37.5)	15 (62.5)	0.32
Female	23 (50)	23 (50)	
Chocolate	1 (20)	4 (80)	0.34
Spicy foods	6 (75)	2 (25)	0.33
Cheese	4 (33)	8 (66)	0.41

disorders, too. The GI disorders were mostly reflux (47.1%), gastric ulcer (17.1%), and gastritis (4.3%). It was demonstrated that 54.3% of migraine patients had history of migraine in their family, mostly in their mothers (20%) or their brothers and sisters (12.9%).

About 48.6% of patients mentioned a special relationship between the outbreak and the severity

of headache on one side and using a special diet on the other side, although the strongest correlation was found for cheese (17.1%), fatty foods (12.9%), and spices (11.4%). Almost 71.4% of patients believed that stress can stimulate the migraine, and 91.4% mentioned that anxiety appeared after the headache. It can also be mentioned that 72.9% of patients had sleep disorders, amongst which insomnia had the highest prevalence (38.6%). About 80% of the patients mentioned a relationship between noise and migraine and 31.4% remembered a relationship between warm weather and the headache. Also 51.9% showed a correlation between light and the headaches and 38.6% had experienced a relationship between the outbreak of headache and different smelling. More than 52.9% mentioned a relationship between the sudden attack and outbreak of headache, and 32.9% were able to differentiate any specific diseases and migraine headaches, particularly digestive disorders as the most prevalent disease. It was demonstrated that 69.5% of women had a correlation between their menstruation and the headache. Frontal headaches, appetite, anorexia state and stress were also mentioned as other problems related to migraine headache (Tables II, IV). At last in order to determine the IgG and IgM antibodies against *H. pylori* in all case and control subjects, the mean optical density (OD) values for both antibodies were calculated. The mean OD value of IgG and IgM antibodies to *H. pylori* was 60.08 ± 7.7 and 32.1 ± 8.7 in the case group, 21.82 ± 6.2 and 17.6 ± 9.4 for the control group, respectively. The prevalence of migraine and the IgG and IgM titre against *H. pylori* were significantly correlated using independent Student's *t*-test ($p \leq 0.048$ and $p \leq 0.03$ respectively).

Discussion

The results of the current study showed a strong correlation between the migraine headache and *H. pylori* infection, GI disorders, blood groups, stress, IgG and IgM titres, social class and some environmental factors. Bigal *et al.*, in a similar study, investigated migraine in 120 000 families using an electronic questionnaire analysing some factors such as age, sex, race, monthly income, marital status and living area. They found that the prevalence of migraine in girls was higher than that in boys, especially in those over 12 years, with a significant difference, as was observed by us in the current study. The prevalence of disease in families with higher annual income was less than that in families with lower annual income, probably due to more stress in low-income families [3], which was in line with the finding of the current study. The results of the current study showed a higher frequency of migraine headache in those with

Table IV. Evaluation of stress and migraine in case and control groups

			Migraine		Total
			No	Yes	
Stress	No	Count	12	8	20
		% within stress	60.0%	40.0%	100.0%
	Yes	Count	20	30	50
		% within stress	40.0%	60.0%	100.0%
	Total	Count	32	38	70
		% within stress	45.7%	54.3%	100%

digestive disorders, as was observed by Meucci *et al.*, who evaluated two studies, one in 378 patients with digestive disorders, and the other on 310 cases in Italy, showing a significant correlation between migraine and digestive disorder in women ($p < 0.006$), while there was no significant correlation between those parameters in men [12]. This finding was further confirmed by a study conducted by IBS medical centre that emphasized a direct relationship between digestive disorders and strength of the migraine headaches. Also from the results of the studies conducted by Movromichalis *et al.* (1995) and Pradier *et al.* (2005), a correlation was observed between migraine and digestive disorder [18, 19].

The current study showed that most migraine patients had some history of migraine in their family, mostly in their mother, brothers and sisters, which is in agreement with the study conducted by Stewart *et al.* in 532 migraine patients and a homogeneous control group [23]. Gervil *et al.* demonstrated that genetic factors play an important role in the aetiology of migraine without aura, with a similar pattern in men and women [12]. The study of Russell *et al.* that was carried out on 378 migraine patients showed that migraine with aura and without aura had different aetiology and it seemed that migraine without aura developed due to a combination of genetic and environmental factors, while migraine with aura was definitely caused and controlled by genetic factors [4], which is somehow in agreement with our results in that the environmental and genetic factors affected the severity of migraine headache.

Olrich *et al.* evaluated migraine in monozygotic and dizygotic twins, finding that the headaches were more prevalent in monozygotic twins than the dizygotes (34% and 12% respectively), with a significant difference, confirming the importance of genetics in outbreak of migraine. Also the risk of recurrent migraine in monozygotes was 50% while in dizygotes it was only 21% [19]. Our study showed a relationship between the outbreak and the severity of migraine headaches in patients

consuming some special meals such as cheese, and fatty foods. Anthony *et al.* evaluated the amount of serotonin in plasma of migraine patients. It was revealed that urinary excretion (5HIAA) which is a serotonin catabolism increased during migraine attacks strongly, confirming our results [1].

Wacogne *et al.* evaluated 141 migraine patients and 109 homogeneous control persons, reporting that stress and anxiety in the case group were significantly more dominant than in the control group, suggesting that stress is one of the main factors for starting and sustainability of migraine attacks [29], as was revealed by us.

Looking at the results of our research, sleep disorders are present in 72.9% of migraine patients, with the highest frequency reported for insomnia. Miller *et al.* also showed that sleep disorders were significantly higher in the case group compared to the control group [20]. The study carried out by Pavia *et al.* on the relationship of headache and sleep disorders on 25 patients with morning and night headaches revealed that migraine and tension headaches were seen in almost half of all sleep disorders [24].

Our study showed that environmental factors such as noise, hot weather, strong light, and different smelling had a serious effect on the outbreak and severity of migraine headache. Many other studies also showed similar patterns, such as the research done by Rabbins *et al.* [25].

One result of the current study was the high prevalence and severity of migraine attacks at the time of menstruation (69.5%). Silberstein in a similar study found that more than 60% of women studied reported a migraine attack at the beginning of menstruation [26]. Also, in another study with the same pattern, migraine attacks with aura in the first 2 days before the beginning of the menstruation, and in the last day of the menstruation, were significantly more frequent than at other times [27]. The difference of IgG and IgM titre between the 2 groups was significant ($p < 0.048$ and $p < 0.03$), indicating a correlation between the antibody titre and the outbreak of

migraine headaches. Tunca *et al.* in their study concluded that 84.6% of patients whose infection was eradicated, and 75% of patients who had benefited from classical treatment, had reduced symptoms of headaches and their headaches were cured [27]. In a study done by Gasbarrini *et al.*, on patients in whom destruction of *H. pylori* was done successfully, a significant difference was observed in reducing frequency, intensity and duration of migraine attacks comparing to those with history of recurrent disease [11]. In another study conducted by Budzyński *et al.*, it was recommended that the *H. pylori* eradication therapy may lead to prolonging the hospitalization-free period in patients suffering from recurrent chest pain [31].

Also, in a study done by Gasbarrini *et al.* in Italy on 225 migraine patients among whom *H. pylori* eradication therapy was performed, it was demonstrated that during 6 months follow-up a significant reduction in frequency, density and duration of migraine attacks was observed [10]. As a result the active *H. pylori* infection is strongly related to the outbreak and severity of migraine headaches, and *H. pylori* treatment reduces migraine headaches significantly. As the infection of bacteria coincides with the severity of the migraine headache and also with the progressive stage of the migraine symptoms, this infection can be considered as one aetiology of the migraine headache.

Finally, according to the results obtained in this study and similar research, the significant difference existing in IgG and IgM antibody titre against *H. pylori* in case compared to control groups shows the importance of studying active *H. pylori* infection in migraine patients, and also gives rise to a hope that definite treatment and eradication of this bacterium can cure or reduce the severity and course of migraine headaches caused by this bacterium significantly if not totally [31], more importantly than other immunological properties [32].

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