

# A Autonomic symptoms in patients with migraine

*Síntomas autonómicos en pacientes con migraña*

<sup>1</sup>Flamerz Arkawazi, Bassam Mahmood; <sup>2</sup>Kareem Hatim, Aqeel; <sup>3</sup>Anwar Alkhazrajy, Lujain

<sup>1</sup>M.B.Ch.B, F.I.C.M.S/ Assist. Prof. of Neurosurgery/Alkindy College of medicine/University of Baghdad.

<sup>2</sup>M.B.Ch.B, F.I.B.M.S/Lecturer Of Neurology/College of Medicine/University of Baghdad.

<sup>3</sup>M.B.Ch.B, F.I.C.M.S Assist Prof./Consultant family physician/ Al kindy College of Medicine /University of Baghdad.

\*corresponding author: Bassam Mahmood Flamerz Arkawazi, 1M.B.Ch.B, F.I.C.M.S/ Assist.t Prof. Of Neurosurgery/Alkindy College of medicine/University of Baghdad, Russia.

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## Abstract

**Introduction:** migraine is a prolonged neurovascular illness. The features by sporadic bouts of acute headache associate with aura or not associated contain various combinations of neurological, gastrointestinal tract, and autonomic variations, with no any indication of main organizational anomalies. Autonomic nervous structure consists of numerous signs and symptoms; nausea, frequent bowel motion, constipation coolness in the upper and lower limbs, tachycardia and thoracic pain. The aim of study to evaluate autonomic purposes in patients with migraine and to assess the autonomic loss function either sympathetic, parasympathetic, or a combination of both. Also, to correlate the severity of this dysfunction with age, sex and migraine kind.

**Methods:** This is a prospective study between May 2009 and May 2019 in the headache clinic at the neuroscience hospital /Baghdad /Iraq. One hundred and twenty person have migraine (84 women and 36 men), the age 15-50 years old, and 60 normal persons as controller collection. The survey paper consist of nervous system debility gauge, cardiovascular reactions examination also done.

**Results:** patients with migraine have incapacitating bouts are disposed to autonomic nervous organism hypo task,

which also is a danger feature for migraine headache, or be a value of common incapacitating bouts. Furthermore, autonomic nervous system loss function and migraine may part a public neural substrate. Rendering to Ewing arrangement of autonomic task examinations, the parasympathetic portion extra exaggerated than the sympathetic portion, significant difference between control group and patients' group, 27% of patients have positive dysautonomia (>2) whereas (73.3%) patients are normal. Tachycardia besides postural faintness are the best recurrent indications in patients have migraine. Migraine and Autonomic abnormal function is more usual also extend sequence of the disease is powerfully connected with autonomic abnormal function which disturbs parasympathetic portion high than sympathetic, for these reasons the autonomic symptoms should be evaluated when assessing the patients with migraine since most of these symptoms are disabling. Conclusions: In patients with migraine, the evaluation of autonomic functions should be a routine work. The cardiac pulse reaction to powerful breath besides valsalva exercise are humble plus useful to assess the parasympathetic portion of autonomic nervous scheme

**Keywords:** Migraine, Sympathetic, Parasympathetic.

## Resumen

**Introducción:** la migraña es prolonga la enfermedad neurovascular. Las características de episodios esporádicos de dolor de cabeza agudo asociado con aura o no asociado contienen varias combinaciones de variaciones neurológicas, del tracto gastrointestinal y autónomas, sin ninguna indicación de anomalías organizacionales principales. La estructura nerviosa autónoma consta de numerosos signos y síntomas; náuseas, deposiciones frecuentes, estreñimiento, frialdad en las extremidades superiores e inferiores, taquicardia y dolor torácico. El objetivo del estudio es evaluar los propósitos autónomos en pacientes con migraña y evaluar la función de pérdida autónoma, ya sea

simpática, parasimpática o una combinación de ambos. También para correlacionar la gravedad de esta disfunción con la edad, el sexo y el tipo de migraña.

**Métodos:** Este es un estudio prospectivo entre mayo de 2009 y mayo de 2019 en la clínica de dolor de cabeza en el hospital de neurociencia / Bagdad / Iraq. Ciento veinte personas tienen migraña (84 mujeres y 36 hombres), de 15 a 50 años de edad, y 60 personas normales como colección controladora. El documento de la encuesta consiste en un indicador de debilidad del sistema nervioso, examen de reacciones cardiovasculares también realizado.

**Resultados:** los pacientes con migraña tienen episodios incapacitantes a los que se somete la hipo tarea del organismo nervioso autónomo, que también es una característica peligrosa para la migraña, o puede ser un valor de los episodios incapacitantes comunes. Además, la función de pérdida del sistema nervioso autónomo y la migraña pueden separar un sustrato neuronal público. Con arreglo a la disposición de Ewing de los exámenes de tareas autónomas, la porción parasimpática extra exagerada que la porción simpática, diferencia significativa entre el grupo control y el grupo de pacientes, el 27% de los pacientes tienen disautonomía positiva (>2) mientras que los pacientes (73.3%) son normales. La taquicardia además del desmayo postural son las mejores indicaciones recurrentes en pacientes con migraña. La migraña y la función anormal autónoma son más habituales, también la secuencia extendida de la enfermedad está fuertemente conectada con la función anormal autónoma que perturba la porción parasimpática más alta que la simpática. Por estas razones, los síntomas autónomos deben evaluarse al evaluar a los pacientes con migraña, ya que la mayoría de estos síntomas son incapacitante.

**Conclusiones:** en pacientes con migraña, la evaluación de las funciones autónomas debe ser un trabajo de rutina. La reacción del pulso cardíaco a la respiración potente, además del ejercicio de valsalva, es humilde y útil para evaluar la porción parasimpática del esquema nervioso autónomo.

**Palabras clave:** Migraña, simpática, parasimpática.

## Introduction

**M**igraine is prolonged neurovascular illness. The features by sporadic bouts of acute headache associate with aura or not associated contain various combinations of neurological, gastrointestinal tract, and autonomic variations, with no any indication of main organizational anomalies<sup>1,2,3</sup>. The migraine pathogenesis is not well understood, although it may be due to defective mitochondrial oxidative phosphorylation, low intracellular magnesium, increase level of neurotoxic amino acid, inherited dysfunction of Ca<sup>2+</sup> channels, or a combination of these factors. This may explain an interictal state of cortical hyper excitability, which is characterized by reduced threshold, and increase that excitability<sup>1,4</sup>. Recently, in positron emission tomography investigation, it was found that there is a spreading oligoemia in the early phase of migraine attacks. During the headache phase, increase in the cerebral blood flow was found in cortical sensory association area and unilaterally in the brainstem, which is considered the pathophysiologic core of migraine with its ascending and descending circuitry, including the ascending pain modulating projection from the midbrain raphe nuclei<sup>5-7</sup>. In 1930, Wolf H. reported on the autonomic nervous sys-

tem involvement in migraine headache<sup>8</sup>. The involvement of the nervous scheme was recommended by numerous symptoms besides signs counting; nausea, frequent bowel motion or decrease bowel motion, increase pulse rate, chest pain and coldness in the extremities<sup>9,10</sup>. In the headache free period, migraine patients have hypo function in parasympathetic nervous system and sympathetic instability<sup>11</sup>. This is clearly reported in migraine patients through spectral analysis of HR fluctuations performed on 10 patients. They also displayed markedly enhanced low frequency fluctuation during day hours and especially at night<sup>12</sup>. The migraine patients with disabling attacks are disposed to to autonomic nervous scheme hypo purpose, which is whichever a danger feature for migraine headache or an importance of recurrent incapacitating bouts<sup>13</sup>. The aim of study is to assess autonomic functions in migraine patients and to evaluate the autonomic dysfunction weather sympathetic, parasympathetic, or a combination of both. Also, to correlate the severity of this dysfunction with age, gender and type of migraine.

## Methods

**O**

ne hundred and twenty patients with migraine were prospectively collected between May 2009 and May 2019 in the headache clinic at the neuroscience hospital /Baghdad /Iraq. Their ages ranged between 15 – 50 years (mean =33.7 years). Eighty-four of them were female and 36 were male patients.

Inclusion criteria were:

1 Patient should have typical criteria for migraine (according to the international headache society criteria for common and classical migraine).

2 The patients should have a normal neuroimaging study (normal brain CT scan or MRI).

Exclusion criteria were:

1 Abnormal neuroimaging study of the patient (brain CT scan or MRI).

2 Patients with features of polyneuropathy.

3 Diabetic patients.

With 60 healthy volunteers from the medical staff, 40 females and 20 males, their age was between 25-45 years as a control group.

The inclusion criteria include for the control group were:

1 No history of headaches

2 No features of polyneuropathy

3 Non- diabetic

A questionnaire paper was used including, autonomic nervous scheme incapacity measure, besides a set of autonomic cardiovascular reactions examination were also realistic.

**Autonomic Function Tests:**

Using 5 standard cardio-vascular Ewing tests<sup>14</sup>, the autonomic function tests were done for all the patients and the control subjects:

1. Immediate HR response to standing.
2. HR response to the VM.
3. HR (R-R interval) variation during deep breathing.
4. Blood pressure (BP) response to isometric handgrip.
5. BP response to standing.

Each one of these tests was given a score: normal=0, border line=0.5, and abnormal=1. The total scores were used for analysis.

Patients with score  $\geq 2$  were labeled as having definite autonomic dysfunction<sup>15</sup>.

The severity of the autonomic dysfunction symptoms was classified according to the autonomic nervous system disability scale<sup>16</sup>.

**Statistical analysis:**

Descriptive analysis in the form of percentage was calculated using Microsoft Office Excel Worksheet and presented in the relevant tables shown below. Chi-Square test was used for statistical analysis by utilizing the Statistical Package for Social Sciences (SPSS) version 17 (p value < 0.05 was considered significant).

**Results**

In this study, we found that common migraine (number= 100/120, 83.3%) was more than classical (number= 20/120, 16.7%), and female (number= 84/120, 70%) were more than male (number= 36/120, 30%). The autonomic symptoms were, in order of frequency, palpitation 56.6%, postural dizziness 51.7%, peripheral flushing 33.4%, and sweating 26.6% (table 1).

**Table 1: The frequency of autonomic symptoms among patients and control**

Autonomic Symptoms	Patients		Control	
	No.	%	No.	%
Palpitation	68/120	56.6	12/60	20
Postural dizziness	62/120	51.7	10/60	16.7
Peripheral flashing	40/120	33.4	6/60	10
Sweating	32/120	26.6	2/60	3.3

The distribution of different autonomic symptoms assessed by autonomic nervous system disability scale for patients and control are illustrated in table 2.

**Table 2: The distribution of different autonomic symptoms**

Autonomic dysfunction symptoms	Patients= 120						Control= 60						P value
	Normal score 0		Mild Score 1		Sever Score 2		Normal Score 0		Mild Score 1		Sever Score 2		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Postural dizziness	58	48.3	48	40	14	11.7	50	83.3	10	16.7	-	-	<0.05
Palpitation	52	43.3	58	48.3	10	8.3	48	80	12	20	-	-	<0.05
Peripheral flushing	80	66.7	38	31.1	2	1.7	54	90	6	10	-	-	<0.05
Sweating	88	73.3	28	23.3	4	3.3	58	96.7	2	3.3	-	-	<0.05

The Results of autonomic function tests among patients and control are illustrated in table 3.

**Table 3: The Results of autonomic function tests**

Autonomic Function Tests	Patient no. 120						Patient no. 30						P value
	Normal		Border Line		Abnormal		Normal		Border Line		Abnormal		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
BP response to standing	108	90	8	6.7	4	3.3	54	90	4	6.7	2	3.3	<0.05
BP response to handgrip	98	81.7	16	13.3	6	5	58	96.7	2	3.3	-	-	<0.05
HR response to deep breathing	78	65	24	20	18	15	54	90	2	3.3	4	6.7	<0.05
HR response to VM	72	60	26	21.7	22	18.3	52	86.6	4	3.3	4	6.7	<0.05
HR response to standing	98	81.7	14	11.7	8	6.7	58	96.7	2	6.7	-	-	<0.05

The Ewing score was  $<2$  in 88/120 (73.3%) of the patients and 58/60 (96.7%) in the control group, and the score was  $\geq 2$  in 32/120 (26.7%) of the patients and 2/60 (3.3%) in the control group ( $p < 0.05$ ). The Ewing score was  $<2$  in 74/100 (74%) of the patients with common migraine and in 14/20 (70%) of the patients with classical migraine, and the score was  $\geq 2$  in 26/100 (26%) of the patients with common migraine and in 6/20 (30%) of the patients with classical migraine ( $p \geq 0.5$ ).

Among the patients with Ewing score of  $<2$  (number=88), the female number was 56 (63.3%) and the male number was 32 (36.4%), while in the patients with Ewing score of  $\geq 2$  (number=32), the female number was 28 (87.5%) and the male number was 4 (12.5%) [ $p \geq 0.5$ ].

In the patients with Ewing score of  $<2$ , the mean age at the onset of illness was 30.02 years and the mean age at the time of investigation was 32.18 years, while in the patients with Ewing score of  $\geq 2$ , the mean age at the onset of illness was 24.38 years and the mean age at the time of investigation was 37.19 years ( $p < 0.05$ ).

**T**his is the first study in Iraqi migraine patients that investigates in details the autonomic function during headache free period. In our study 120 patients were classified according to the type of migraine, 100 (83.3%) of them were common migraine, including 68 (68%) female and 32 (32%) male, while 20 (16.7%) of them were classical migraine including 16 (80%) female and 4 (20%) male. Our study showed that common migraine was more common than classical migraine and female were affected more than male. These results are comparable with other similar studies<sup>1,17-20</sup>. We found that the most common autonomic symptoms (table 1) were palpitation (56.6%), postural dizziness (51.7%), peripheral flushing (33.4%), and sweating (26.6%). All these symptoms are common complaint in our patients specially palpitation and postural dizziness which makes the patient apprehensive. The high prevalence of autonomic symptoms found among our patients in this study should alert the clinician to assess carefully these symptoms in the evaluation of migraine patients and not only emphasizing on the usual features of migraine. These symptoms may be disabling and overcoming them will improve the quality of life of the patients. As demonstrated in table 2, according to the autonomic nervous system disability score, the patients were divided into normal score=0 (no autonomic symptoms), mild score=1 (transient autonomic symptoms), and server score=2 (persistent autonomic symptoms). Our study showed that most of our patients have transient symptoms, while few have severe symptoms, which is important statistically in evaluation to the controller. Rendering to Ewing et al organization of autonomic function tests (table 3), the most fre-

quent abnormality encountered in our patients were HR response to VM (40%), and HR response to deep breathing (35%)<sup>8</sup>. These results were statistically significant in comparison to the control, while the other tests were not significant. This leads us to think that the parasympathetic portion of autonomic nervous scheme is exaggerated additional than the sympathetic portion and this similar to the results of other studies<sup>11,13</sup>. This may be explained by that, the autonomic nervous system imbalance that plays a pathophysiological role in migraine. This imbalance considered a danger factors for headache due to migraine or a consequence of recurrent bouts. Furthermore, nervous scheme dysfunction besides migraine may have the same neural substrate<sup>13</sup>. Rendering to the Ewing mark, (27%) of current patients presented with fixed dysautonomia ( $\geq 2$ ), but 88 (73%) of patients were usual. This was statistically significant. This leads to the conclusion that the autonomic dysfunction is not a rare complication of migraine but unfortunately, there is no available study to compare with. This study showed no significant difference between the severity of autonomic dysfunction in both types of migraine (common and classical), and gender. Our study also showed that the patients with Ewing score of  $<2$ : the mean age at the onset of illness was 30.02 years, and the mean age at the time of investigation was 32.18 years, while the patients with Ewing score of  $\geq 2$ : the mean age at the onset of illness was 24.38 years and the mean age at the time of investigation was 37.19 years. This was statistically significant. This concludes that the younger the patients are, the more is the need to use tests capable of detecting subtle changes in autonomic function. Alternatively, it could be explained by the fact that the longer the duration of the disease, the more likely that the autonomic function will be affected as in other diseases like diabetes.

## Conclusions

In patients with migraine, the evaluation of autonomic functions should be a routine work. The cardiac pulse reaction to powerful breath besides valsalva exercise are humble plus useful to assess the parasympathetic portion of autonomic nervous scheme.

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