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ORIGINAL ARTICLE

The Serum C - reactive protein Level and Monocyte Count assessment among Adult Migraine Patients

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ABSTRACT

Background: Migraine is a highly prevalent and frequently disabling condition. Its etiology is multifactorial, involving various genetic, environmental and inflammatory factors, hence, it is reasonable to assess the serum C-reactive protein level and monocyte count in migraine.

Objective: Assessment of the serum C-reactive protein level and monocyte count among migraineurs.

Subjects and Methods: This case-control prospective study was conducted on twenty-seven migraineurs attended the Neurology Outpatient Clinic of Zagazig University Hospital and diagnosed according to The International Classification of Headache Disorders, (3rd edition) and twenty-seven controls. All subjects underwent: Detailed medical, neurological and headache history, complete general and neurological examination and investigations: complete blood count (including monocyte count), liver and kidney function tests, lipid profile, blood glucose level, erythrocyte sedimentation rate, C-reactive protein level , electrocardiography and computed tomography brain and/or magnetic resonance imaging brain when indicated.

Results: Migraine patients without preventive treatment had higher C-reactive protein level and monocytes count in comparison to others with treatment however; the difference was not a statistically significant. We can notice also that there is no correlation between monocyte count and C-reactive protein. In our study the monocyte count showed a statistically significant higher values in case group than control also, was a statistically significant area under the curve and cut off of monocyte regarding detection of cases >550, with sensitivity, specificity, +ve predictive, -ve predictive and accuracy were 81.5%, 59.3%, 66.7%, 76.1% and 70.3% respectively.

Conclusion: Our findings suggest that the elevated C-reactive protein level and monocyte count are associated with migraine.

Key words; C-reactive protein, Monocyte count, Migraine.

INTRODUCTION

Migraine could be an extremely current and frequently disabling condition that poses an interesting medical and economic burden on human society. It is a complex, multifactorial neurological disorder affecting about 10% of the adult population worldwide and it's the second most prevalent neurological disorder and therefore the causal agent of incapacity in below the 50s [1].

Migraine is defined as a perennial unilateral headache disorder lasting 4–72 hours, characterized by pulsing pain of moderate or severe intensity, related to nausea and/or photophobia and phonophobia [2].

Migraine has two major subtypes. A migraine with aura (classic type) is primarily characterized by the transient focal neurologic symptoms that usually precede or sometimes accompany a headache and migraine without aura (common type) [3].

Migraine etiology is complex, involving both numerous genetic and environmental factors, however scientists think about three necessary mechanisms for its pathophysiology including: inflammatory, neurological and cardiovascular impairments [4]. It is accompanied by the evidence that a migraine is considerably related to cardiovascular disorders, coronary

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cardiopathy and stroke [5].

Among the varied inflammatory biomarkers, the C - reactive protein (CRP) and monocyte count are powerfully related to cardiovascular disorders, coronary cardiovascular disease and cerebral stroke [6]. Hence, it's reasonable to investigate the role of the serum C - reactive protein (CRP) level and monocyte count during a migraine.

AIM OF THE WORK

Assessment of the serum CRP level and monocyte count among migraine patients.

SUBJECTS AND METHODS

This case-control prospective study was conducted on twenty-seven migraineurs who attended the Neurology Outpatient's Clinics of Neurology Department in Zagazig University Hospital during the period (from November 2017 to April 2019) and twenty-seven age and sex-matched healthy controls. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The subjects included in the study: Case group: Migraine patients diagnosed according to The International Classification of Headache Disorders, 3rd edition [7] and **Control group**: Healthy individuals with age and sex matching and no history of migraine or in their first degree relatives.

The inclusion criteria: Age of the subjects must be above 18 years old. **The exclusion criteria:** Applied to both case and control groups include: Obesity with body mass index (BMI) $\geq$ 30 kg/m^2, hypercholesterolemia, hypertension, diabetes mellitus, active infection, history of cardiovascular disease, subjects on anti-inflammatory drugs, pregnancy & lactation, immune diseases and smoking.

The ethical consideration: According to ethical rules of institutional review board (IRB) Informed consent from patients about the study was obtained and no harmful maneuvers performed or used for any patients.

All subjects in this study underwent: Detailed medical, neurological and headache history was taken, complete general examination and complete neurological examination.

The laboratory investigations: The samples were collected through 72 hours from last migraine attack. Routine laboratory investigations include: Complete Blood Count (CBC): Including Monocyte count, liver and kidney function tests, lipid profile, blood glucose level and Erythrocyte Sedimentation Rate (ESR). Specific laboratory investigations include: C-reactive protein (CRP) test, electrocardiography (ECG) and neuroimaging computed tomography (CT) brain and/or magnetic resonance imaging (MRI) brain when indicated.

Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis [8].

RESULTS

Table (1): C-reactive protein (CRP) and monocyte distribution between groups.

From table (1) we can notice that migraine patients had a statistically significant higher monocytes count in comparison to control. The patient showed higher levels of CRP than control however; the difference was not reaching the statistically significance.

Table (2): Area under the curve and cut off of monocyte regarding detection of migraine.

From table (2) we can notice that there was a statistically significant area under the curve with cutoff >550.

Table (3): Association between monocyte cutoff and migraine.

From table (3) we can notice that there was a statistically significant association between monocyte cutoff and cases (P = 0.002).

Table (4): Validity of monocyte cutoff for detection of migraine.

From table (4) we can notice that sensitivity, specificity, +ve predictive, -ve predictive and accuracy were 81.5%, 59.3%, 66.7%, 76.1% and 70.3% respectively.

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Table (1): C-reactive protein (CRP) and monocyte distribution between groups

	Case (N=27)	Control (N=27)	t/ Mann Whitney	P
CRP	5.1±2.8	4.17±1.17	1.688	0.097
Monocyte	677.77±145	533.3±188.1	3.160	0.003*

CRP: C-reactive protein * : Statistically highly significant
P value was set at <0.05 for significant results

Table (2): Area under the curve and cut off of monocyte regarding detection of migraine

Area Under the Curve				
Test Result Variable(s): Monocyte				
Area	Cutoff	P	95% Confidence Interval	
			Lower Bound	Upper Bound
0.728	>550	0.004*	0.590	0.866

* : Statistically highly significant P value was set at <0.05 for significant results

Table (3): Association between monocyte cutoff and migraine

	cutoff		Groups		Total	X^2	P	Kappa agreement
			Control	Case				
Monocyte	<550	N	16	5	21	9.42	0.002*	0.52
		%	59.3%	18.5%	38.9%			
	>550	N	11	22	33			
		%	40.7%	81.5%	61.1%			
Total		N	27	27	54			
		%	100.0%	100.0%	100.0%			

(X^2): Chi square test * : Statistically highly significant
P value was set at <0.05 for significant results

Table (4): Validity of monocyte cutoff for detection of migraine.

	Sensitivity	Specificity	+VE Predictive	-VE predictive	Accuracy
Monocytes	81.5%	59.3%	66.7%	76.1%	70.3%

DISCUSSION

Migraine could be a primary headache disorder characterized by perennial headaches that are moderate to severe. Typically, the headaches have an effect on one half of the head, are beating in nature, and last from two to seventy two hours [9].

The precise mechanisms stay unclear, however a neurovascular inflammation as a part of the complicated pathophysiological method has been steered. Migraines also are believed to be due to a combination of environmental and genetic factors [10].

Among the varied inflammatory biomarkers, the C - reactive protein (CRP) and monocyte count are powerfully related to vessel disorders, coronary cardiovascular disease and cerebral stroke [6], [11], hence, it's reasonable that's why the study was chosen to be conducted to investigate the role of the CRP level and monocyte count in migraine.

Our study showed higher levels of CRP in cases than controls that was distributed as 5.1±2.8 in case group and 4.17±1.17 in

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control respectively, however the difference did not reach the statistically significance.

This in agreement with a review of studies published between 2006 and 2014 indicated higher CRP levels in people with migraine than in controls [12].

Furthermore, study conducted by Yildiz et al., [13] found that CRP level was considerably higher in migraine group, and reported that higher serum inflammatory markers support the role of inflammation in migraine pathogenesis.

The association of CRP level with migraine has been shown in a little of case control studies of migraine with vascular risk factors [14], [15], [16].

Avci et al., [15] reported that serum CRP levels were considerably higher in migraine patients than control subjects.

In contrast with the present study, another study reported that no association between CRP levels and migraine [16].

The effectiveness of biomarkers is often measured in terms of their sensitivity, specificity and by making receiver in operation characteristic curves, which permit for the calculation of the area under the curve. Sensitivity is commonly defined as the proportion of a population with a disease in whom the check in question offers a positive result. Specificity is that the proportion of that population while not the sickness in whom the check offers a negative result. Biomarkers that are sensitive have low false-negative rates and people that are extremely specific have low false-positive rates. Optimally, a good biomarker are going to be each sensitive and specific. It's terribly rare that a diagnostic biomarker is strictly present or absent. Much more commonly, the presence of a biomarker is measured as a continuous variable and cutoffs are defined along that continuum to establish the presence or absence of disease [17].

In the present study the monocyte count showed a statistically significant higher values in case group than control also, was a statistically significant area under the curve and cut off of monocyte regarding detection of cases >550 which means when monocyte count more than 550 is significant as an inflammatory marker in migraine patients.

There was significant association between monocyte cutoff and cases (P = 0.002), with sensitivity, specificity, +ve predictive, -ve predictive and accuracy were 81.5%, 59.3%, 66.7%, 76.1% and 70.3% respectively.

This adapted to study led by *Peng et al.*, [18] who announced that monocyte count in patients with migraine was higher than control groups.

Pusic et al., [19] reported that microglia may play an important role in neuropathic pain and migraine initiation by neuroinflammatory mediators, and a thought of current monocytes as direct microglia orthologous was introduced in neuroinflammatory processes. Additionally, neuroinflammation will be mirrored by peripheral monocytes changes in some neurologic diseases.

In fact, monocytes in peripheral circulation will populate the central nervous system and differentiate into microglia below conditions of neuropathic inflammation and a potential relationship between increased levels of CRP and migraine has been well established [12]. Taken together, the above evidences cause a hypothesis with reference to peripheral monocyte count and CRP in patients with migraine.

Therefore, our findings suggest that elevated monocyte count and CRP are associated with migraine.

CONCLUSION

In conclusion the present study showed a statistically significant higher values of the monocyte count in case group than control which mean that monocyte count may play a role in inflammatory theory of migraine as a biomarker in pathogenesis, diagnosis and prognosis of migraine. The higher levels of C-reactive protein as a non-specific marker of inflammation in cases than controls also support the inflammatory theory of migraine. These markers may help us to understand the pathophysiology of migraine also, because the low cost of these tests that commonly used, they may be beneficial for guarding migraine patients against long-term comorbidities.

The limitations were a relatively small sample size in the present study. In addition, the levels of monocyte count were not assessed in other migraine

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subgroups.

Our recommendations are future researches for better understanding of mechanisms of migraine and pathogenesis to reveal the actual underlying causes and the association between migraine and inflammatory biomarkers for developing better treatment with satisfied outcome.

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