

Evaluation of the level of interleukin 18 in migraine patients in Diyala Governorate: Focus on Cancer

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ABSTRACT Migraine is a severe headache that comes in the form of attacks and is felt in one side of the head, and sometimes on both sides. It is accompanied by nausea, vomiting, and phobia of light and noise. Migraines have been classified into two main types: migraine without aura (MO) and migraine with aura (MA). There are many genetic, environmental and immunological factors that contribute to the occurrence of migraines, and migraines affect about (10-12%) of individuals at some time in their lives. This study was conducted in the period from October 15, 2022 to March 22, 2023, when 50 blood samples were collected from patients with migraine disease in private pathological analysis laboratories in several areas of Diyala Governorate. The study included the age group from (14-56) years, as it was The number of males is 13 and the number of females is 37. Also, 38 blood samples were collected from healthy people of both gender and used as a control group. The number of males was 25 and the number of females was 13 within the age group (18-56) years. The study included assessing the level of IL-18 concentration using ELISA Technique.

The study found that the incidence of migraine in females was 74.0% higher than that of males, with an average age of (28.95 ± 1.37) years, with a statistically significant difference between the gender with a value of $(P > 0.05)$. The results of the current study showed a slight increase in the level of IL-18 concentration in patients with migraine by $(0.32 \pm 0.02 \text{ pg/ml})$ compared to the control group $(0.31 \pm 0.01 \text{ pg/ml})$ and there is no statistically significant difference under the probability $(P > 0.05)$. Conclusion: This study concluded that the incidence of migraine is higher among females than males. IL-18: Interleukin is an important regulator of innate and immune responses and is involved in slowing the pain process, including neuropathic pain. Therefore, it is an anti-inflammatory cytokine, and a decrease in its concentration leads to an exacerbation of the severity of pain in migraine patients.

Key words: Migraine, IL-18, ELISA

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INTRODUCTION

Migraine is a chronic disorder of the brain and blood vessels, usually characterized by moderate to severe headache attacks, accompanied by nausea, vomiting, and phobia of light and noise. Approximately one-third of migraine patients also experience transient neurological symptoms called migraine aura. Migraine poses a significant social and economic burden, and is classified as the most disabling disorder in women under the age of 50, with the prevalence being the highest. The global prevalence of migraine has increased dramatically over the past three decades. According to the 2019 Global Burden of Disease (GBD) study, the estimated global prevalence of migraine increased from 721.9 million in 1990 to 1.1 billion in 2019 [1-4].

Migraine has been classified into two main types: migraine without aura (MO) and migraine with aura (MA), with visual, sensory, or other Central Nervous System (CNS) symptoms preceding the headache. Migraines are highly prevalent, affecting 12% of the population, and attacking up to 17% of women and 6% of men annually. Among children, this disease tends to occur when Girls more than boys. Interleukin-18 is an immune stimulating cytokine that belongs to the IL-1 family, IL-18 can regulate both innate and adaptive immune responses through its effect on Natural Killer (NK) cells, monocytes, dendritic cells, T cells, and B cells. IL-18 acts synergistically with other pro-inflammatory cytokines to enhance IFN- γ production. By natural killer cells, T cells, and possibly other cell types. Systemic administration of IL-18 has been shown to have antitumor activity in several experimental animal models. Phase I clinical trials of reconstituted human IL-18 have shown that it can be safely administered to patients with advanced cancer. Biological effects of IL-18 treatment include activation of monocytes, natural killer cells, and T cells and production of IFN- γ as well as other cytokines in vivo. IL-18 appears to function predominantly as a co-stimulatory cytokine and may be optimally used for cancer immunotherapy in combination with other immune cytokines, vaccines, or monoclonal antibodies [5-7].

IL-18 is produced as an inactive precursor (pro IL-18), activated by cysteine cleavage by the protease caspase-1. Closely related to IL-1B, IL-18 has had a major role in Immunity, tumor growth, inflammation, and even the pain process in various rodent models, IL-18 has been found constitutively expressed in microglia, and

has been shown to mediate the interaction of microglia and astrocytes, contributing to neuropathic pain and cancer pain [8-15].

MATERIALS AND METHODS

Study Samples

This study was conducted in the period from October 15, 2022 to March 22, 2023, when 50 blood samples were collected from patients with migraine disease in private pathological analysis laboratories in several areas of Diyala Governorate. The study included the age group from (14-56) years. The number of males was 13 and the number of females was 37. Also, 38 blood samples from apparently healthy people of both sexes were collected and used as a control group. The number of males was 25 and the number of females was 13 within the age group (18 - 56) years. 5 ml of venous blood for the study samples was drawn using medical syringes, and the blood was placed in test tubes for the purpose of separating the serum, then immunological tests were performed on it, then the level of IL-18 was measured using the ELSA test according to the instructions of the kit from Mybiosource Company.

Test principle

This test used a number of ready-made enzymes according to the immunoassay technique where an enzyme-linked immunosorbent assay (ELISA) test was used to estimate the level of incubated IL-18 and then, biotin-labeled anti-IL-18 antibodies were added to bind to the HRP, leading to the formation of the immune complex. After incubation, the plate was washed and the substance was added to stop the reaction, thus turning the solution from blue to yellow, and the absorbance was measured at a wavelength of 450 nm.

RESULT AND DISCUSSION

Figure 1 shows the rates of migraine incidence by gender. The current study included 50 patients with migraine in Diyala Governorate, with an average age of (28.76±1.46) years. The number of males was 13, with a percentage of (26.0%), and the number of females was 37, with a percentage of (74.0%). As for the control group, it included 38 apparently healthy people with an average age of (28.95±1.37) years. The number of males was 25 (65.8%) and the number of females was 13 (34.2%) with a highly significant difference between the sexes with a statistical significance under probability P<0.001) as well shown in Table 1.

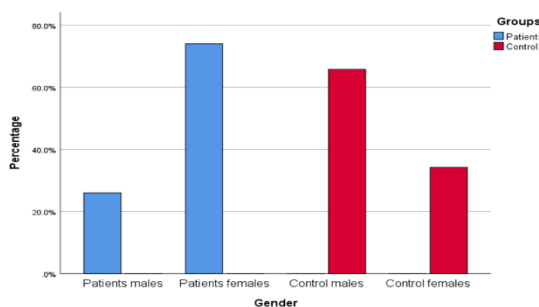


Fig 1. The incidence of migraine according to gender

Tab 1. the percentage of migraine incidence among the study groups according to gender

Gender	Patient group number (%)	Healthy group number (%)	Probability
male	(26.0)13	(65.8)25	P<0.001
female	(74.0)37	(34.2)13	P<0.001
total summation	(100.0)50	(100.0)38	

This study indicated that the incidence of migraines in females is higher than in males. This study agreed with a study conducted by Lipton, who found that the incidence of migraines in females is greater than in males, with a prevalence rate of 17.1% in females and 5.6% in males. Our study also agreed with Mohammadi et al. 2023 stated that females are more susceptible to migraines, and also agreed with Sakai that the prevalence of migraines in women is 4.4 times higher than in men. This study indicated that the incidence of migraines in females is higher than in males. This study agreed with a study conducted by Lipton, who found that

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tension and physical stress, and its elevation It causes anxiety, high pressure, heart rate, and high blood cholesterol, as well as genetic predisposition, as there are a number of genes related to migraine research [20, 21].

Level assessment IL-18

Figure 2 shows the results of the current study, which was conducted on 88 samples divided into two groups: 50 samples

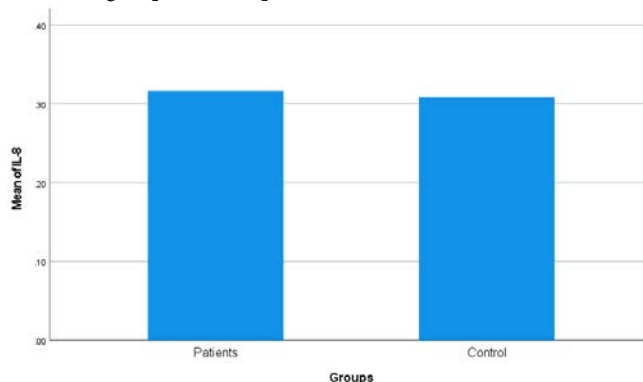


Fig 2. The measurement of the level of IL-18 in the study group

Tab 2. The average level of IL-18 concentrations in the study group

Probability	(pg/ml) IL-18 average level		Gender
	Healthy group	Patients group	
P > 0.05	0.31 ± 0.02	0.35 ± 0.08	Male
P > 0.05	0.32 ± 0.02	0.30 ± 0.01	Female
P > 0.05	0.31 ± 0.01	0.32 ± 0.02	total summation
	P > 0.05	P > 0.05	Probability

The reason for the slight increase is that IL-18, an important regulator of innate and immune responses and is involved in slowing the pain process, including neuropathic pain, cancer, and alleviating nociceptive behavior Therefore, it is an anti-inflammatory cytokine, and its low concentration leads to worsening pain intensity in migraine patients. While our study did not agree with the study [22-25].

A significant increase in IL-18 was recorded in migraine patients. This was attributed to the important role of IL-18 in the pathophysiology of migraine and the pain attacks associated with it. In a study, they considered IL-18 to be a pro-inflammatory cytokine and its serum levels have been confirmed to be increased in individuals with migraine and genetic variants of IL18 have been shown to have an effect on susceptibility to migraine. Its A -105 and -137G alleles, the main cytokine producers, increased the chances of developing the disease by 53.0% and 46.0%, respectively [27]. In a study conducted on animals, they found an increase in the concentration of IL-18 and IL-1B in the cerebral cortex of the animals [28]. In a study, they found an increase in the concentration of IL-18 in microglia and astrocytes. These inflammatory changes led to the cognitive impairment associated with migraines [29].

with migraine disease and 38 apparently healthy samples. It showed a slight increase in the level of IL-18 concentration in patients with migraine, as its concentration reached (0.32±0.02 pg/ml) compared to the healthy group, where it reached (0.31±0.01 pg/ml). No statistically significant difference was recorded under the probability (P> 0.05) as in Table 2.

CONCLUSION

This study concluded that the incidence of migraine is higher among females than males. IL-18: Interleukin is an important regulator of innate and immune responses and is involved in slowing the pain process, including neuropathic pain. Therefore, it is an anti-inflammatory cytokine, and a decrease in its concentration leads to an exacerbation of the severity of pain in migraine patients.

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