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Research Article

Evaluation of the level of interleukin 22 in patients with migraine in Diyala Governorate

Mohammed Nasser*, Ibtisam Badday Hassan, Wissam F. Hassan

Biology Department, College of Education for Pure Science, The University of Diyala, Iraq
Email: muhammadaljumaily19941994@gmail.com

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Abstract

A migraine is a severe headache that comes in the form of attacks and is felt in one side of the head. It is usually not constant on one side but rather changes from one side to the other with repeated attacks, and sometimes on both sides and in most cases it is localized, that is, in the temple or around the eye. 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 was 13 and the number of females was 37. Also, 38 blood samples from apparently healthy people of both genders were collected 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 evaluating the level of interleukin 22 concentration using ELISA Technique. The study found that the incidence of migraine in females was 74.0% higher than in males percent 26.0%, with an average age of (28.76±1.46 years), compared to healthy people, where the average age was (28.95±1.37 years), with highly significant and statistically significant difference between the gender under the probability ($P < 0.001$). The results of the current study showed a noticeable increase in the level of interleukin 22 concentration in patients with migraine, with a ratio of 2.33 (2.25 - 2.85 pg/ml) compared to the healthy group, which reached 2.23(2.51 - 2.14 pg/ml), which recorded a highly significant difference with statistical significance under Probability($P<0.001$). The results of the current study showed a noticeable increase in females, where the concentration of IL-22 reached 2.35 (2.26 - 2.85 pg/ml), compared to males, where it reached 2.33 (2.25 - 2.51 pg/ml), which recorded a highly significant difference ($P<0.001$). The study concluded that IL-22 plays a role in cellular targeting and signal transduction to initiate and selectively regulate immune responses and also plays a central role in inflammatory diseases such as psoriasis and systemic lupus erythematosus.

Keywords: migraine, IL-22, ELISA technique

Introduction

Migraine is a chronic neurological disorder characterized by the recurrence of moderate to severe headaches, often in combination with a number of symptoms of the autonomic nervous system. It is usually characterized by moderate to severe headache attacks, accompanied by nausea, vomiting, and a fear of light and noise. Approximately 1-3 of migraine patients also experience a transient neurological symptom called a migraine aura (Arnold, 2018). 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 (Prakash, 2018). Migraines are highly prevalent, affecting 12% of the population, and attacking up to 17% of women and 6% of men annually (Stewart et al., 2008; Vetvik and Macgregor, 2017). Among children, this disease tends to occur more frequently in females than in males. (Macgregor,2017).

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 (Safiri et al., 2022). IL-22 is a member of the IL-10 family of cytokines and represents an important response factor for activated Th22, Th1, and Th17 cells, as well as subsets of Tc cells, T cells, and natural killer (NK) cells , and NKT cells (Wolk et al., 2010). IL-22 is involved in both wound healing and protection against microbes. Dysregulation of IL-22 is implicated in many autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and psoriasis (Pan et al., 2013).

The biological activity of IL-22 is initiated by binding to a cell surface complex composed of IL-22R1 and IL-10R2 receptor chains and is further regulated through interactions with a soluble binding protein, IL-22BP, which shares structural sequence similarity with IL-22. extracellular region of IL-22R1 (SIL-22R1), IL-22 and IL-10 receptor chains play a role in cellular targeting and signal transduction to initiate and selectively regulate immune responses(Jones et al., 2008). Different cells in both innate and acquired immunity produce IL-22, but the primary sources are T cells. Th22 cell is a new CD4+ T cell line, which has differentiated from naïve T cells in the presence of various pro-inflammatory cytokines including IL-6. IL-22 inhibits IL-4 production. It also has essential functions in protecting the mucosal surface and repairing tissues (Shabgah et al., 2017).

Material 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 (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 wine-filled medical syringes, and the blood was placed in test tubes containing gel for the purpose of separating the serum, then immunological tests were performed on it, then the level of IL-22 was measured using an ELISA test according to the kit's instructions from Mybiosource.

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-22 and then, biotin-labeled anti-IL-22 antibodies were added to bind to the HRP, resulting in 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 No. (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 gender with a statistical significance under probability (P<0.001) As shown in the table (1).

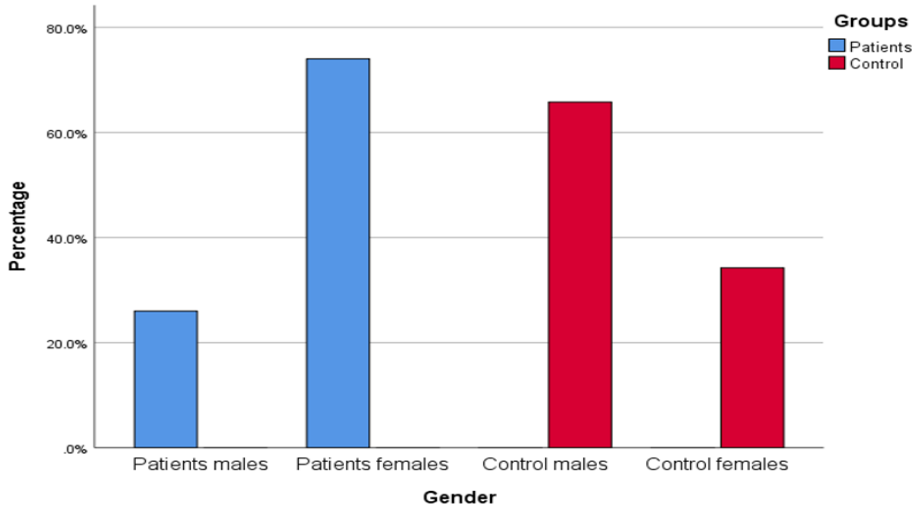

Figure 1. The incidence of migraine according to gender

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

Probability	Healthy group number (%)	Patient group number (%)	Gender
P<0.001	(26) 13	(26) 13	**Male**
P<0.001	(34.2) 13	(74) 37	**Female**
	(100) 38	(100) 50	**Total**

This study indicated that the incidence of migraines in females is higher than in males. This study agreed with a study conducted by Lipton et al. (2007), 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). Females are more susceptible to migraines, and our study also agreed with Sakai et al. (2022) that the prevalence of migraines in women is 4.4 times

higher than in men. These studies explained that the reason for the higher incidence in females could be largely related to the fluctuation in the level of sex hormones in women. During the menstrual cycle, pregnancy, and periods of menopause, as well as non-sexual hormones, such as the adrenal cortex hormone cortisol, which plays a major role in controlling psychological tension and physical stress, and its elevation causes anxiety, high pressure, heart rate, and high blood cholesterol, as well as genetic predisposition, as there are a number of genes for it. Relevance to migraine research (Pavlovic, 2019; Kamil, 2020).

Measuring the level of IL-22

Figure (2) shows the results of the current study, which was conducted on 88 samples divided into two groups: 50 patients with migraine onset and 38 samples from apparently healthy people, which recorded a significant increase in the level of IL-22 concentration, reaching 2.33 (2.25 - 2.85 pg/ml) compared to the healthy group, where It reached 2.23 (2.14 - 2.51 pg/ml), it was recorded a highly significant difference with statistical significance and under probability ($P < 0.001$). It also recorded a high significant difference between males and females with statistical significance under probability ($P < 0.001$). As shown in the table (2).

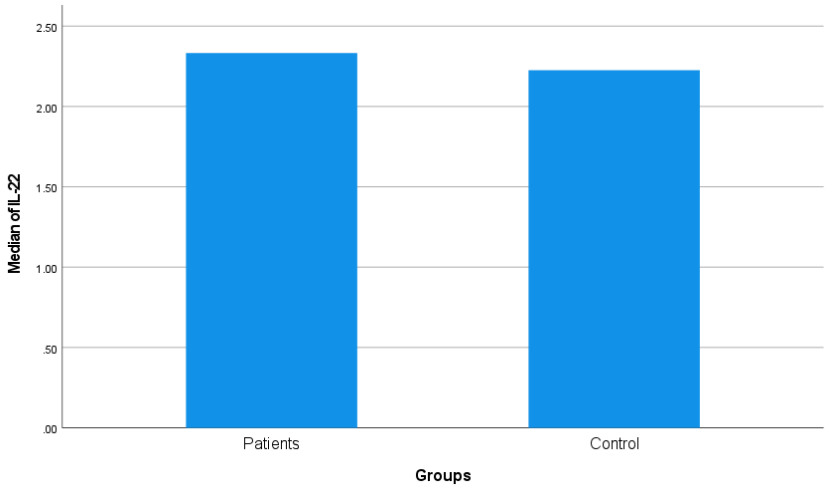

Figure 2. The measurement of the level of IL-18 in the study group

Table 2. The average level of IL-22 concentrations in the study group

Probability	(pg/ml) IL-22average level		Gender
	Healthy group	Patients group	
P < 0.001	2.20 (2.14 – 2.51)	2.33 (2.25 – 2.51)	Male
P < 0.001	2.26 (2.15 – 2.41)	2.35 (2.26 – 2.85)	Female

P < 0.001	2.23 (2.14 – 2.51)	2.33 (2.25 – 2.85)	total summation
	P > 0.05	P > 0.05	Probability

The study is considered the first of its kind on the relationship of IL-22 to migraine disease in Iraq and the world, according to the limits of the researcher's knowledge, and therefore there is no comparative study of it only through studies on other diseases. The study conducted by Chinannan (2017) . Regarding hepatitis B virus infection with cirrhosis, the levels of interleukin 22 in patients with hepatitis B virus infection and cirrhosis were much higher than the levels of patients with simple hepatitis B virus. Also, in a study on rheumatoid arthritis conducted by Leipe et al (2011). It was found that IL-22 levels were high compared to the healthy group, indicating the possible involvement of IL-22 in the pathophysiology of rheumatoid arthritis. In another study conducted by Tufman et al. (2016) on patients suffering from lung cancer and other lung diseases, the concentration of IL-22 was higher in patients suffering from pneumonia than in the healthy group. IL-22 was found to act mainly on epithelial cells. In the skin, it mediates keratinocyte proliferation and epidermal hyperplasia and plays a central role in inflammatory diseases such as psoriasis. It is a distinct product of Th17 cells. It is also secreted at functionally significant levels by other immune cells, especially NKp44/NKp46-expressing natural killer (NK) cells and lymphoid tissue stimulating cells following IL-23 and IL-22 stimulation. It is a member of the IL-10 family of antioxidants and also an inflammatory cytokine. Which mediates epithelial immunity as IL-22 expression is enhanced in the inflamed colon mucosa of individuals with inflammatory bowel disease. It acts mainly on epithelial cells eg. Liver cells, where they favor antimicrobial defense, regeneration, and protection against damage and stimulate acute phase reactants and some chemical compounds (Turner et al., 2010; Mizoguchi et al., 2018; Keir et al., 2020).

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