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Estimation of cytokine level IL - 4, IL - 12, IL-17 and some immune features among patients with Herpes zoster in Thi-Qar Province / Southern Iraq

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***Abstract*—Varicella-zoster virus (VZV), which was dormant in the dorsal root ganglia or cranial nerve, reactivates to produce the viral illness shingle. Immunosenescence, which includes the documented decline of cell-mediated immunity with aging, can result in the VZV reactivation. While Herpes Zoster(HZ) is typically mild in young, persons who are in good health, while older individuals are more likely to experience complications. The present study was carried out during July 2022 to January 2023 in the province of Thi-Qar We estimate the levels of VZV IgG , IL-4, IL-12,IL-17 and checking level vitronectin (VTN) in the blood of 70 HZ patients who did not suffer from superinfection. 30 individuals of a comparable age who were healthy and free of infectious and inflammatory diseases made up the control group. blood samples were collected from them and examined via the ELISA system. While the plasma vitronectin level dropped in HZ patients when in comparison to the control group, both the serum levels of the cytokines IL-4, IL-12, and IL-17 as well as the VZV IgG titer considerably rose. According to the results, HZ patients without chronic illnesses had significantly greater levels of IL-17. compared to individuals suffering from chronic illnesses. Additionally, IL-12 levels were noticeably higher in females than in males. Age and sex differences were not found to be significantly different in the research.**

***Keywords*— VZV , Herpes zoster , Cytokine , VTN**

I. INTRODUCTION

Chickenpox and shingles are brought on by the VZV. Clinical and epidemiological studies show that following a childhood case of chickenpox , the VZV latently grows in the dorsal root ganglia and is reactivated many years later in adults to produce zoster[1]. HZ can affect anyone of any age, but older persons are more likely to develop it. To accurately manage the outbreak and avoid serious complications like the virus spreading to the central nervous system, a diagnosis must take into account the patient's medical history. [2]. Varicella recovery is linked to VZV-specific T cell-mediated immunity (VZV-CMI), which is crucial for avoiding HZ by restricting the reactivation and replication of latent VZV[3]. HZ is a condition that affects the sensory ganglion, nerve, and epidermis locally and is brought on by the reactivation of VZV from latency and subsequent replication. HZ typically affects only the dermatome and causes a single dorsal root or cranial nerve ganglion, which innervates it, to produce radicular pain and a vesicular rash. [4]. Independent of the prevalence of varicella, HZ virus infection happens sporadically throughout the year without a seasonal pattern. The host's VZV-CMI, which preserves VZV latency, is the primary element affecting the host-virus interaction and determines the incidence of HZ[5]. However, this chance increases to one in two for those who are 85 years of age or older [6].In fact, the likelihood of developing HZ rises significantly after age 50, with people 50 years or older accounting for two-thirds of HZ cases [7]. Anyone who has experienced varicella is susceptible to HZ, and in Europe, more than 90% of adolescents under the age of 15 have varicella [8]. The main cause of aging-related increases in VZV reactivation rates is decreasing T cell populations, not declining humoral immunity [9] T cells are necessary for treating VZV disease, reducing its severity, and preventing reactivation, but humoral immunity provided by antibodies is necessary for preventing original VZV infection[10].

II. PATIENTS AND METHODS

In total, 70 HZ patients were included in the present research. The samples were obtained from a dermatological consultant at Al-Nasiriyah Teaching Hospital between July 2022 and January 2023. The research also included 30 healthy people as a control group. From each patient, 5 mL of blood were drawn, which was collected under sterile conditions and divided into 3 ml and put in a gel tube and 2 ml in an EDTA tube. The sample was centrifuged for 10 minutes at 4000 rpm, The serum and plasma were then separated and distributed in an Eppendorf tube, which was then stored at -20 for use in immunoassays. Before starting the work, all components, including serums, plasma, and

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reagents, were placed at room temperature, and. The ELISA technique was used to determine the levels of cytokines and proteins. The reagents used in this study are from the Bioassay Company in China.

A. Ethical consideration

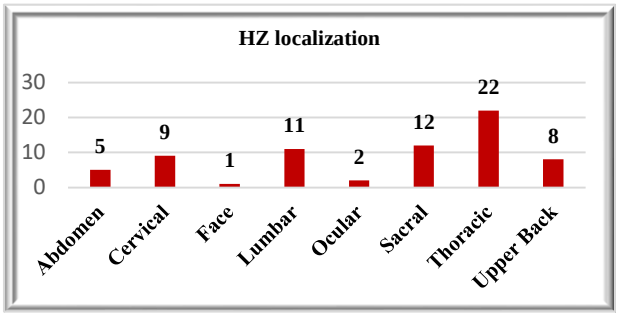
A study was conducted based on the ethical standards followed by the Ministry of Health in Iraq, and after describing the study's goal to each patient, a verbal consent was acquired. This study received ethical approval by the University of Thi-Qar (No. 101/02).

Abbreviations__ Varicella-zoster virus (VZV), Herpes Zoster(HZ), vitronectin (VTN),

III. RESULTS

The serum levels of IL-4, IL-12, and IL-17, as well as VZV IgG were statistically higher in HZ patients in contrast to the control group. While the plasma level of vitronectin in patients is statistically lower than in control.

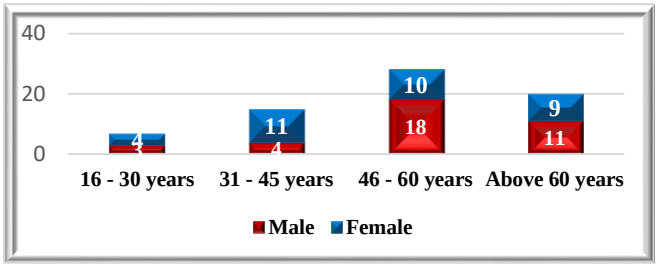
According to the current results, the highest infection rates were found in the thoracic region (31%), While the face had the lowest infection rate (1%), the research also found a statistically significant difference in VZV infection according to body site at p. value 0.05, as shown in figure1.



CalX$^{2=}$ 35.6 TabX$^{2=}$ 14.07 DF= 7 p. value < 0.001**

Figure 1: HZ infection according to body site infection.

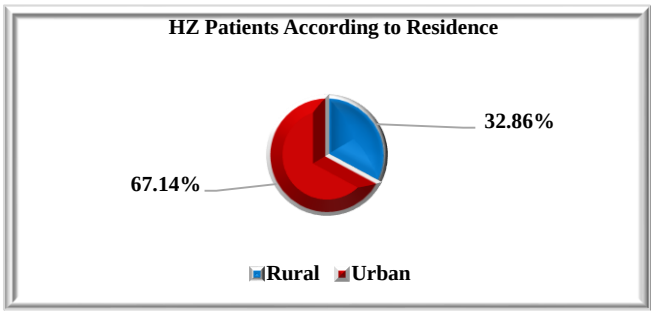
The current findings revealed that 51.4% of males were infected with Varicella-zoster, while 48.6% of females were. It was also discovered that a third age group (46-60)years had a high infection rate, while the age group (16-30)years had the lowest infection rate. The study also noted a non-significant statistical difference between Varicella-zoster infection and age groups and sex at p. value < 0.05, as in figure 2.



CalX$^{2=}$ 5.84 TabX$^{2=}$ 7.81 DF= 3 p. value 0.120^{NS}

Figure 2: HZ patients according age groups and sex.

The current results showed a 67.14% of infection in patients that habitat urban whereas the rural patients 32.86%, the study also noted a significant statistical difference between Varicella-zoster infection and residence of patients at p. value < 0.05, as in figure 3.



CalX$^{2=}$ 8.22 TabX$^{2=}$ 3.84 DF= 1 p. value 0.004**

Figure 3: HZ patients according to residence

In the current research, the level of VTN increased considerably in the control group compare to the HZ patients, the levels of IL-4,IL-,IL-12,IL-17 and VZV IgG increased significantly in the HZ patients compared to the control group at a p. value <0.05. as shown in table 1.

TABLE1: IMMUNE PARAMETER LEVEL IN HZ PATIENTS AND THE CONTROL GROUP.

Immune Parameters	Patient No. 70	Control No. 30	t test *p. value*
	Mean ± SD		
VZV IgG	2.63 ± 0.95	0.45 ± 0.17	< 0.001**
IL-4	371.9 ± 94.1	66.1 ± 19.3	< 0.001**
IL-12	21.2 ± 7.94	4.80 ± 1.95	< 0.001**
IL-17	209.1 ± 69.5	32.8 ± 7.77	< 0.001**
VTN	231.7 ± 79.1	443.9 ± 121.6	< 0.001**

(** highly significant)

The current research found no significant difference in the concentration of any of the immune parameters involved according to sex in HZ patients, Except for IL-12, which was significantly higher in HZ-infected females than HZ-infected males, at p. value < 0.05 as in table 2.

TABLE 2: LEVELS OF IMMUNE PARAMETERS IN HZ PATIENTS ACCORDING TO SEX.

Immune Parameters	Patients Female No. 34	Patients Male No. 36	t test *p. value*
	Mean ± SD		
VZV IgG	2.54 ± 0.95	2.72 ± 0.95	0.440
IL-4	367.3 ± 94.6	376.3 ± 94.8	0.694
IL-12	23.6 ± 8.22	19.0 ± 7.04	0.013*
IL-17	204.9 ± 69.1	213.0 ± 70.5	0.627
VTN	235.6 ± 86.6	228.1 ± 72.4	0.694

The present study showed that the concentration of IL-17 was obviously higher in patients without chronic disease than in patients with chronic disease, but that the concentration of other immune parameters was not significantly different in HZ patients according to chronic disease at (p. value < 0.05) as in table 3.

TABLE 3:LEVELS OF IMMUNE PARAMETERS IN HZ PATIENTS

ACCORDING TO CHRONIC DISEASE.

Immune Parameters	With chronic disease No. 15	Without No. 55	t test *p. value*
	Mean ± SD		
VZV IgG	2.44 ± 0.92	2.69 ± 0.96	0.373^{NS}
IL-4	398.3 ± 67.4	364.8 ± 99.4	0.137^{NS}
IL-12	19.2 ± 7.60	21.8 ± 8.00	0.259^{NS}
IL-17	178.0 ± 51.5	217.6 ± 611.7	0.022*
VTN	233.1 ± 67.3	231.4 ± 72.6	0.933^{NS}

IV. DISCUSSION

Cytokines, important immune response mediators, enable the integration of cellular activity with immune responses. The externalization of cellular defense also depends on cytokines. The serum cytokine levels of HZ participants IL-4, IL-12, and IL-17 were measured in this research. The relationship between latent VZV infection and the immune system is thought to depend heavily on T cells. It is currently unknown what pathogenetic process triggers VZV reactivation from latency. The cellular immunological response is the most efficient immune barrier against VZV infection. According to this research, the thoracic region had the highest infection rate 31.4% and the face had the lowest infection rate 1.4%. Figure 1. The results of this study were in agreement with those of Rampakakis et al [11], who did research in eight countries across North America, Latin America, and Asia and found that 48% of thoracic patients had the highest levels of infection. While The results of this research contrasted with those of Nasser HA et al[12], who investigated the risk factors for herpes zoster in the Thi-Qar Governorate and found that sacral 32%, thoracic 16%, and foot 4%. This variation might result from various sample sizes, sample collection sites, or sample collection circumstances.

The study findings recorded that there are 51.4% of infected males and 48.6% of infected females. and this agreed with Nasser HA et al. [12], who studied 50 cases of shingles and found that excess incidence was more common in males 60% than in females 40% in the Thi-Qar Governorate. Although the difference was not Significant. Our findings are in contrast with a study by Yan Li et al. [13] that was performed in China as well as other studies[14,15] that discovered a higher annual incidence rate in females than in males. Even though some research found no statistically significant difference between male and female incidence. The existence of gender variations must therefore be confirmed through additional research[16,17].

The current findings showed that urban patients had 67.14% of infections, compared to rural patients' which had 32.86% infection, Additionally, these findings demonstrated that the variations are highly significant P .value< 0.05. The findings of this study concurred with Nasser HA et al[12], who found that metropolitan areas had a greater prevalence rate than rural areas, Similar results were reported in an earlier investigation that discovered a statistically significant difference in the prevalence of HZ between participants living in urban and rural areas[18,19]. The VZV IgG, IL-4, IL-12 and IL-17 of patients with HZ were significantly elevated compared to the control group, as a result of VZV reactivation and emergence of HZ lesions, resulting in an increased number of interferon antibodies, were This result is consistent with Zajkowska A et al and Zak-Prelich M et al; [20, 21]. One of the important Extracellular matrix proteins with multiple functions found in plasma is known as (VTN). Numerous cellular processes were highlighted, including angiogenesis, plasminogen activation, and cell adhesion [22].This result was in agreement with Wang T et al.'s study of 40 HZ patients by ELISA, which observed Reduced plasma levels of VTN in patients with HZ[23]. In contrast to the control group, the HZ patients had a significantly lower concentration of VTN, according to the current study.

In line with studies of the level of IgG in the herpes virus group, which did not find any statistically significant differences in the level of VZV IgG based on sex[24,25], the results of this study did not find any statistically significant differences in the level of VZV IgG in HZ patients according to sex. While there was no statistically significant difference in IL-4 levels between males and females with HZ infection, IL-12 levels were noticeably greater in females. In the current study, a non-significant difference in IL-17 levels between males and females was also discovered. According to the findings of a study on the assessment of levels of inflammation in the blood and fibrinolysis, including VTN, age, and gender had no discernible influence on these[25]. With the exception of IL-12, which was considerably greater in HZ-infected females than males, none of the immunological markers studied in this study showed a significant sex-based variation in concentration. This may imply that women have greater levels of IL-12 due to hormonal and physical differences or because IL-12 is involved in reducing the inflammatory burden on erythropoiesis. However, the study found that regardless of the patient's gender, the amount of cytokines and other immune proteins in HZ patients did not differ significantly between men and women.

The current research found a non-significant difference in the concentrations of IL-4, IL-12, and VTN in HZ patients according to chronic disease, but a significant increase in IL-17 concentration in patients without chronic disease compared to patients with chronic disease. The results of the present research demonstrated that chronic illnesses did not have the same impact on the level of cytokines in HZ. These may be brought on by a patient's environment, a chronic disease's bad lifestyle stage, or the tiny sample size of HZ patients who have a chronic disease, who account for 21.4% of all patients. However, we were unable to locate research that examined the level of cytokines in HZ patients who had a chronic illness in the literature.

V. CONCLUSIONS

It was found that the levels of cytokines involved in humoral and cell-mediated immunity had risen. These findings support a broad immune system activation encompassing both humoral and cell-mediated immunity . The study showed that HZ infections are more common in urban than in rural regions, and did not find a relationship between the Covid-19 vaccination and the occurrence of the disease.

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