Immunopathological role of Interleukins-17 in COVID-19Patients with related to Pfizer vaccine

Ruaa Kareem Surhan[1] and Mayyada F Darweesh[2]
[1]College of health and medical techniques, kufa, Al-Furat Al-Awsat Technical University, 31003 Al-Kufa, Iraq.
[1]Email: ruaa.surhan@atu.edu.iq
[2]Department of Microbiology, Faculty of Science, University of Kufa, Iraq
[2]Email: mayada.alsagheeri@uokufa.edu.iq

ABSTRACT
Background: COVID-19 pandemic with 603,711,760 confirmed cases and 6,484,136 reported deaths but vaccines led to in an eminent reduction in disease associated morbidity and mortality.IL-17 immunologically plausible as a strategy to prevent acute respiratory distress syndrome (ARDS) in COVID-19
Material and method: The present research consisted of 160 participants who were divided into two groups as80 Covid-19(vaccination and unvaccinated) patientsand 80 healthy subjects(vaccinated and unvaccinated) control group during January - April 2022. Blood samples collected from all subjects to separated serum to measure IL-17 by ELISA assay
Result: The findings of this research show that there are significantly more male patients than female patients, and the age distribution between 41-50 had the greatest frequency, in both covid-19 groups . The current investigation found that unvaccinated patients had considerably higher concentrations of IL-17 (pg/ml) than vaccinated groups.

Keywords: Interlukin-17,vaccination, Coronavirus disease.

1-INTRODUCTION

One of the many public health programs that helps keep people healthy is immunization (Lopez *et al*., 2023). Avaccine is any biological preparation used to induce protective antibodies against a disease. In the 18th century, an English country doctor named Edward Jenner pioneered the idea of vaccination by protecting his patients against smallpox using pus from cowpox-infected milkmaids (Sehume, 2011). BioNTech, a German biotech firm, created Pfizer, a COVID-19 vaccine based on messenger RNA. In 2021, the first COVID-19 vaccination will be appropriate through the Nourishment and Medication Management (FDA). The Pfizer-BioNTech Vaccines are currently available under the brand name Comirnaty of prevention COVID-19 in those aged 12 and above (Gasmi *et al*.,2022). COVID-19 is caused by a kind of virus called a coronavirus, and researchers have known about human coronaviruses since the 1960s. Patients with COVID 19 frequently have lower respiratory infection symptoms that are connected to the respiratory system in addition to upper respiratory symptoms such a dry cough, fever, and dyspnea (Atwah *et al*., 2022). IL-17 is a key inflammatory cytokine produced mainly by Th17 cells which have pleiotropic and crucial roles in innate and adaptive immune responses that involve complicated intracellular signal pathways that leads to the activation of various pro-inflammatory cytokines and chemokinesduring infection , autoimmune disease , it is a member of the inflammatory cytokine family that can exert both host-protective and pathological effects (Kang et al., 2021)dysregulated production of IL-17 contribute to lung damage and hypercoagulability inpatients with severe COVID-19.

2- MATERIAL AND METHODS

A case – control study were done for 80 patients with covid-19 disease (who have positive result to (PCR) nasopharyngeal swab for SARS-2) during the period from 1st January 2022 to 1stApril 2022 with both sex which attended to Al-Najaf AL-Ashraf National center for COVID-19 screening in AL-Amal hospital at first weak infection with symptoms (fever ,loss of smelling & testing, Headache, nasal congestion) as repeated by WHO

guide (Wei *et al.*,2020), the patients divided according to vaccination into two groups 40 patients unvaccinated and 40 patients vaccinated . In addition to 80 apparently healthy subjects as control group divided into two groups 40 vaccination healthy and 40 unvaccination healthy.Two ml of blood were collected from all subjects to separated serum that used to measured IL-17 serum level according to company protocol (Elabscience, USA).

Statistical Analysis

Statistical analysis was carried out by using statistical software (IBM SPSS Statistics 26). The quantitative data given as mean ± SE and the differences tested by t-test (two means) and one-way ANOVA test (more than two means). Probability of (P≤ 0.05) was measured to be significant statistically (Alsadawi et al., 2022).

3-RESULT AND DISCUSSION

According to the results of this study, the male patients outnumbered the female patients by a margin of 26(65 %) to 14(35 %) for unvaccinated patients and 24(60%) vs 16(40%) for vaccinated patientscompare to 21(52.5%) vs 19(47.5%) as Vaccinated healthy and 20(50%) vs 20(50%) as unvaccinated healthy as show in (Figure 2). The age distribution of unvaccinated patients that 41-50 had the highest frequency and those aged 21-30, who had the lowest frequency, which were 17 and 2 , the distribution of vaccinated patients that show 41-50 had the highest frequency and those aged 61-70, who had the lowest frequency, which were 14(35%) and 2(5%), respectively and so on. Figure (2)
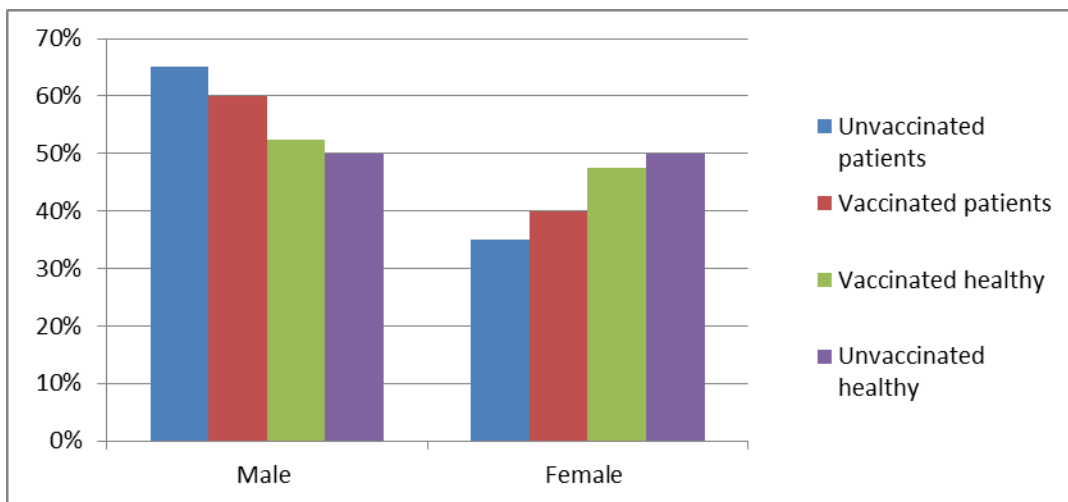

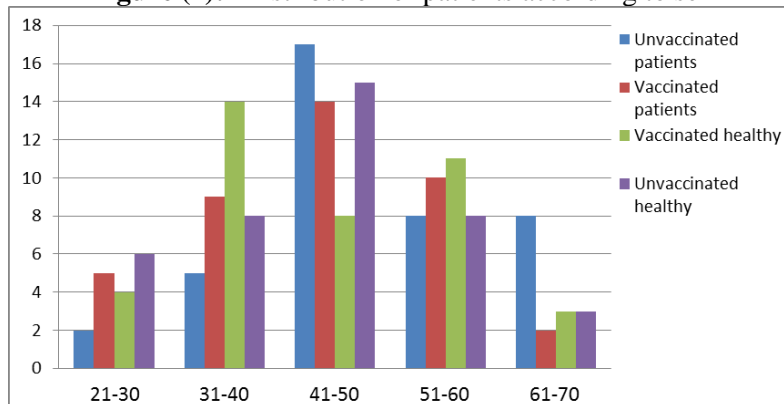**Figure (1):-** Distribution of patients according to sex

**Figure (2):-** Distribution of the patients according to the age group

Many researchers observed that the severity and the risk of death due to COVID-19 disease is increased with the age and the comorbidity increases up to 49 % in critical cases (Wu and McGoogan, 2020). The prevalence of critical individuals with SARS due to COVID-19 was 63.93% in men and 36.07% in women and indicated that in-hospital critical state or death was associated with the age of >60 year , the explanation is that aging leads to impaired functioning of multiple body systems, including the immune system, which is a factor involved in increased mortality due to COVID-19 in the elderly (Carvalho et al.,2023). The sex hormones can also affect the immune and inflammatory modulator during infection. The estrogen promotes both innate and adaptive immunity, while testosterone (a male hormone) in its turn has a suppressive effect on immune function(Cattrini et al., 2020). Age could strongly predict the fate of COVID-19 disease (Saghazadeh & Rezaei ,2020) who reported that elderly population is at increased risk of developing and dying from COVID-19 and revealed that the mean age of COVID-19 patients is 52.4 years while , children and adolescents are the least likely group to be infected with the COVID-19 occurring in only 2% of patients 19 years of age or younger , they observed ven if they get sick, they will get a mild form of disease without serious complications, with an average probability of 0.2% of dying. This results about male: female frequency nearly similar to study by (Devaux et al., 2023) who suggested that male more vaccinated than female but females develop higher antibody response post-vaccination compared to males, and vaccine responses are diminished in older adults due to immune senescence. Also , Bayram et al. (2021) showed that seropositivity was higher among females (84.6%) than males (70.6%), after the first dose (1D) of CoronaVac. The median age of the unvaccinated patients was 62 years, and there was no statistically significant variation between the sexes, as described by (Jin et al.,2020).

Evaluation of interlukin-17 (IL-17) in COVID-19

The present study observed in Figure (3) that the concentration of IL-17A was increased in Covid-19 patients in compare to healthy control (284.1 ± 12.84; 52.51 ± 2.258) pg/ml . Also, the present study observed in Figure (4) that the concentration of IL-17A was5 folded higher in unvaccinated Covid-19 patients in compare to unvaccinated healthy (284.1 ± 12.84; 52.51 ± 2.258) pg/ml and six folded increased Vaccinated patients 315.3 ± 22.94 pg/ml than unvaccinated healthy . The results observed that IL-17 serum concentration higher in Pfizer vaccinated healthy compare to unvaccinated healthy (250.5 ± 36.74, 52.51 ± 2.258)pg/ml.
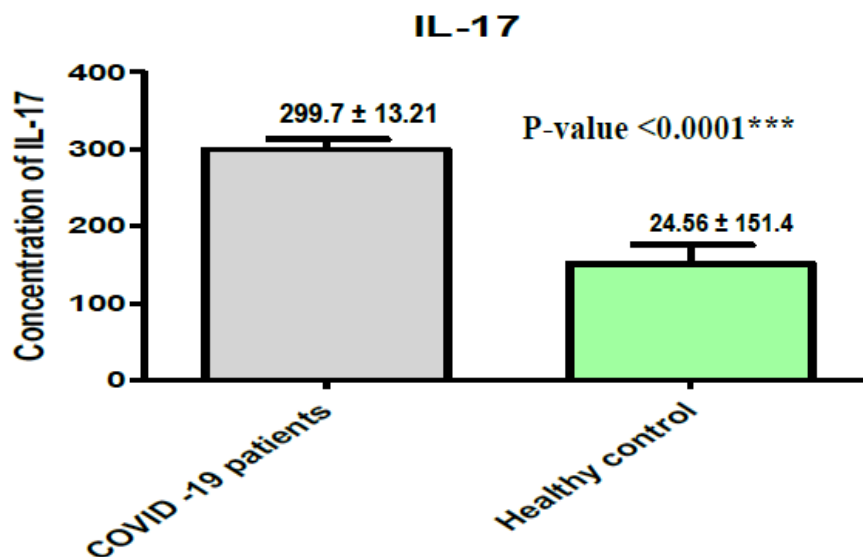
Figure(3): Concentration of IL-17A in serum of COVID-19 patients and healthy control
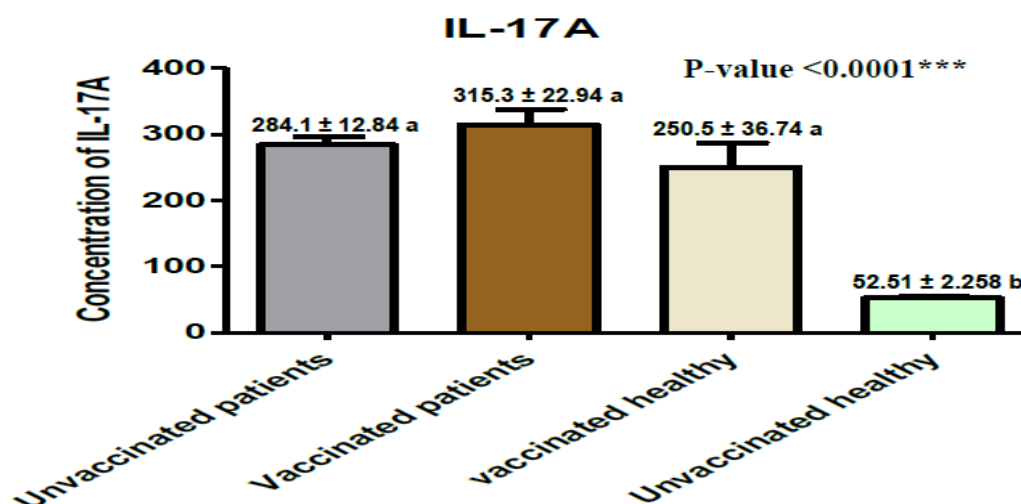
Figure(4): Concentration of IL-17A in serum of unvaccinated COVID-19 patients , vaccinated patients, vaccinated healthy and unvaccinated healthy.

The different letters indicate the existence of significant differences
Elevated levels of Th17 cells and circulating IL-17 in the peripheral blood of severely SARS-CoV-2 infected individuals are consistent with the findings of (Abd and Darweesh,2023) whom observed that a significant increase ($p < 0.05$) in mean serum level of IL-17 in patients compare to healthy group, and the mean critical - server cases higher than Mild-Moderate cases (101.79, 74.83, and 27.65) pg/mL. Also,(Bulat *et al*., 2021) they found that high amounts of pro-inflammatory cytokines IL17 are also involved in COVID-19 immunopathogenesis. Also, serum levels of IL-17 were found to be significantly higher in unvaccinated patients than in healthy controls (Liuet al., 2020), because of IL-17 may be associated with disease intensity and development, they verified that IL-17 plays a role in the clinical results of patients with COVID-19. Similarly, (Gong et al., 2020) noted an association between elevated IL-17A levels, a Th17 response in COVID-19 patients' upper and lower respiratory tracts, and the disease's severity. Ghazavi et al., (2021) who confirmed that Th17 (IL-17) cytokines concentration were increased in COVID-19 pneumonia patients , and mention that IL-17 involved in inducing and mediating proinflammatory responses.According to Pfizer vaccination , (Schulthei et al.,2022) they found a highly elevation in IL-17A, IL-1 β, TNF-α in unvaccinated covid-19 patients than in vaccinated patients who were exposed to the SARSCoV-2 virus via natural COVID-19.(Karaba et al.,2022)the median levels of baseline cytokines IL- 17 and IL-16, in the Healthy group were lower than Covid-19 patients in both vaccinated and unvaccinated patients IL-17, IL-16, IL-18and IL-12.

 Pacha *et al*.,(2020) they mention that excessive production of IL-17 in Covid patients led to destruction of the lung parenchyma through maladaptive neutrophil recruitment and through the prevention of apoptosis due to the induction of granulocyte colony-stimulating factor expression , they suggested that IL-17 inhibition has been adopted as a common and successful strategy to reduce the injury associated with inflammatory effect of IL-17. In Kirkuk city -Iraq by (Ali et al.,2023)a high significant difference ($P <0.01$) between the patients (101.79±27.13) pg/mL and the control group (58.39±11.15) pg/mL concerning IL-17. Also, (Kadhim et al.,2023)shown that IL-10 serum levels significantly decreased in the 4th month of the 2 nd dose of the Pfizer BioNTech vaccine for healthy volunteer and these results explain the important role for IL-10 can regulate the cytokine storm response in severe COVID patients by inhibiting IL-6, IL-1β, and IL-17 and blocking IL-12 that highly elevated in Covid patients .

3721

CONCLUSION

The current results concluded that the female patients by a margin is less than male and The age distribution of unvaccination COVID-19 patients that 41-50 had the highest frequency and those aged 21-30. The levels of IL-17 were found to be increase in COVID-19 patients than health group and vaccinated COVID-19 patientslower than unvaccinated patients and this elucidate the efficacy of vaccine in regulate immune response in patients by regulates cytokines production and prevent the cytokines storm .

REFERENCES

Lopez SM, Sato AI, Chatterjee A. Vaccines: An overview. Viral, Parasitic, Bacterial, and Fungal Infections. 2023 Jan 1:699-717.

Sehume KL. Childhood immunization in Mmakaunyane village in the North West Province of South Africa (Doctoral dissertation, University of Limpopo (Medunsa Campus)).

Gasmi A, Srinath S, Dadar M, Pivina L, Menzel A, Benahmed AG, Chirumbolo S, Bjørklund G. A global survey in the developmental landscape of possible vaccination strategies for COVID-19. Clinical Immunology. 2022 Feb 24:108958.

Atwah B, Iqbal MS, Kabrah S, Kabrah A, Alghamdi S, Tabassum A, Baghdadi MA, Alzahrani H. Susceptibility of Diabetic Patients to COVID-19 Infections: Clinico-Hematological and Complications Analysis. Vaccines. 2023 Mar 1;11(3):561.

Kang YW, Lee SC, Jeon SM, Jo EK. Roles of Interleukin-17 and Th17 Responses in COVID-19. Journal of Bacteriology and Virology. 2021 Sep 30;51(3):89-102.

Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic transmission of SARS-CoV-2—Singapore, january 23–march 16, 2020. Morbidity and Mortality Weekly Report. 2020 Apr 4;69(14):411.

Alsadawi AA, Alammar M, Hamid M. The Role of TLR-4 (896A/G) Gene polymorphisms in patients with Diabetic foot ulcer. Al-Kufa University Journal for Biology. 2022;14(3):118-27.

Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. jama. 2020 Apr 7;323(13):1239-42.

Carvalho VP, Pontes JP, Neto DR, Borges CE, Campos GR, Ribeiro HL, Amaral WN. Mortality and associated factors in patients with COVID-19: cross-sectional study. Vaccines. 2023 Jan;11(1):71.

Cattrini C, Bersanelli M, Latocca MM, Conte B, Vallome G, Boccardo F. Sex hormones and hormone therapy during COVID-19 pandemic: implications for patients with cancer. Cancers. 2020 Aug 18;12(8):2325.

Saghazadeh A, Rezaei N. Immune-epidemiological parameters of the novel coronavirus–a perspective. Expert review of clinical immunology. 2020 May 3;16(5):465-70

Devaux CA, Camoin-Jau L. Molecular Mimicry of the Viral Spike in the SARS-CoV-2 Vaccine Possibly Triggers Transient Dysregulation of ACE2, Leading to Vascular and Coagulation Dysfunction Similar to SARS-CoV-2 Infection. Viruses. 2023 Apr 25;15(5):1045.

Bayram A, Demirbakan H, Günel Karadeniz P, Erdoğan M, Koçer I. Quantitation of antibodies against SARS-CoV-2 spike protein after two doses of CoronaVac in healthcare workers. Journal of medical virology. 2021 Sep;93(9):5560-7.

Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, Liu S, Yang JK. Gender differences in patients with COVID-19: focus on severity and mortality. Frontiers in public health. 2020:152.

Abd SA, Darweesh MF. Interleukin-10 gene polymorphism in COVID-19 patients and outcome of disease. HIV Nursing. 2023 Feb 9;23(2):912-7.

Bulat V, Situm M, Azdajic MD, Likic R. Potential role of IL-17 blocking agents in the treatment of severe COVID-19?. British Journal of Clinical Pharmacology. 2021 Mar;87(3):1578.

Liu Y, Zhang C, Huang F, Yang Y, Wang F, Yuan J, Zhang Z, Qin Y, Li X, Zhao D, Li S. Elevated plasma levels of selective cytokines in COVID-19 patients reflect viral load and lung injury. National Science Review. 2020 Jun 1;7(6):1003-11.

Gong J, Dong H, Xia QS, Huang ZY, Wang DK, Zhao Y, Liu WH, Tu SH, Zhang MM, Wang Q, Lu FE. Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study. BMC infectious diseases. 2020 Dec;20:1-7.

Ghazavi A, Ganji A, Keshavarzian N, Rabiemajd S, Mosayebi G. Cytokine profile and disease severity in patients with COVID-19. Cytokine. 2021 Jan 1;137:155323.

Schultheiß C, Willscher E, Paschold L, Gottschick C, Klee B, Henkes SS, Bosurgi L, Dutzmann J, Sedding D, Frese T, Girndt M. The IL-1β, IL-6, and TNF cytokine triad is associated with post-acute sequelae of COVID-19. Cell Reports Medicine. 2022 Jun 21;3(6):100663.

Karaba AH, Zhu X, Liang T, Wang KH, Rittenhouse AG, Akinde O, Eby Y, Ruff JE, Blankson JN, Abedon AT, Alejo JL. A third dose of SARS-CoV-2 vaccine increases neutralizing antibodies against variants of concern in solid organ transplant recipients. American Journal of Transplantation. 2022 Apr;22(4):1253-60.

Pacha O, Sallman MA, Evans SE. COVID-19: a case for inhibiting IL-17?. Nature Reviews Immunology. 2020 Jun;20(6):345-6.

Ali MR, Abed SM, AL-Izzi MH. The Role of IL-6 and IL-17 in SARS CoV-2 Patients with Secondary Bacterial Pneumonia. Tikrit Journal of Pure Science. 2023 Feb 20;28(1):15-20.

Kadhim AA, Abdullah AR, Alshuaikh AM. Reduction of IL-10 Serum Level after 4 Months of Pfizer-BioNTech Vaccine Administration of 2nd Dose in Students at Al-Iraqia University. The Egyptian Journal of Hospital Medicine. 2023 Jan 1;90(2):2308-10.