Evaluation the Role of CD4 and CD8 Reducing the Deterioration of COVID-19 Iraqi Patients

Aya Ahmed Saeed[1], Layla Fouad Ali[2]

[1,2]University of Baghdad, Department of Biology, College of Science, Baghdad, Iraq.

Abstract

Since its start spreed "Severe acute respiratory syndrome coronavirus 2" was discovered in Wuhan, China.that is chargeable COVID-19, a pandemic virus, has end up a widespread fitness hassle everywhere in the global Over 2.1 million people have been affected. We analyze serum concentration of CD4 marker and CD8 marker depend in COVID-19 sufferers, and to make clear a relationship between these variables and disorder Progression and severity For those purpose, (158) sufferers with COVID-19 (showed with the aid of using polymerase chain reaction) and (22) seemingly wholesome human beings have been protected withinside the present day examine and taken into consideration as a manipulate group. All examine population (sufferers and manipulate) have been subjected to the assessment of serum awareness of CD4 marker and CD8 marker. COVID-19 sufferers displayed a huge elevation withinside the tiers of parameters protected on this examine while in comparison with wholesome controls. We additionally observed that concentration of CD4 and CD8 high in sever (CD4 5.68 ±0.16-CD8 961.74 ±49.48) than critical (CD4 4.76 ±0.14- CD8 880.19 ±52.03)and moderate (CD43.83 ±0.09 – CD8 647.52 ±44.54) groups with high significant different (P≤0.01(.

Keywords: corona virus, covid-19, CD4 marker, CD8 marker.

INTRODUCTION

One of the viruses is the Coronavirus.primary viruses which often stirring the respiration gadget in people (chen et al., 2020). In December of this year, Atypical Unknown Pneumonia was discovered. turned into Wuhan, Hubei Province, was the first place where it was discovered Excessive temperature (over 38°C), coughing, lethargy, breathing problems have all gone reported in patientsCOVID-19 has been assigned to the contamination, which has been linked to a seafood market in Wuhan, China. (Zhu et al.,2020;wn et al.,2020). It swiftly spread to various nations in Far East Asia, then to the Middle East and Europe. In severe circumstances, the sickness can lead to pneumonia, septic shock, metabolic acidosis, and bleeding were seen. (Helmy et al., 2020). The incubation length has been rated from 5 - 14 days and might range from affected person to affected person in keeping with age and contamination history (Xiao et al.,2020) . According to study, both symptomatic and asymptomatic individuals are capable of transmitting COVID-19 through nasal droplets and direct contact (Lauer et al ., 2020;Xiao et al.,2020;Chan et al .,2020). Currently, there is neither a vaccination nor therapy that is beneficial for COVID-19 infections; nevertheless, a number of preventive health practices can help patients alleviate their most pressing concerns. (Khedmat, 2020). On sixteen March 2020, the sickness affected extra than a hundred and fifty nations & regions all across the globe There has been a notable rise in COVID-19 times during the last few months. On the 24th of February The first verified incidence of Covid-19 infection in Iraq was reported in the governorate of Najaf in 2020. a scholar who had arrived previously from Iran. (Al-Suhail and Ali , 2020),found with the resource of the usage of 4 times from one very own On the 25th of February, a family in Kirkuk province received a trip data to Iran. On February 27 in Baghdad, a second incidence involving a victim who had recently visited Iran was reported. (OCHA. IRAQ, 2020). seventy 4 confirmed times and 8 fatalities have been cautioned at some stage in Iraq as of 12 March 2020 (OCHA. IRAQ, 2020). The cases increased to 1,415 on April 16, 2020, and 78 fatalities were documented. (OCHA. IRAQ, 2020). By 24 May 2020, the showed instances of COVID-19 reached 4469 and pronounced a hundred and sixty deaths, at the same time as 2738 sufferers recovered from the infection (OCHA. IRAQ, 2020). The virus SARS-CoV-2 (or 2019-nCoV) causes This virus is a member of the B branch of the coronavirus genus. (Zhu et al., 2020). Coronaviruses are positive-sense, single-stranded RNA viruses with a genomic size of 30 kb that are contained. The viral pp1a-pp1b replicase, the 3C-like protease (3CLpro), the papain-like protease (PLpro), and the RNA-based RNA-polymerase are all encoded by the SARS-CoV-2 genome RdRp (Fehr and Perlman, 2015; Zhou et al., 2020). Spike (S), Envelope (E), Matrix/Membrane (M), Matrix/Membrane (M), Matrix/Membran When a virulent illness Inhaled virus infects respiratory epithelial cells; DCs phagocytoze the virus and provide antigens to T lymphocytes. Cytotoxic CD8+ T cells produce and release

pro-inflammatory cytokines that induce cell death, while effector T cells differentiate by killing infected epithelial cells. (Rogers and Williams, 2018 Both activated CD8+ cells and anti-MERS-CoV antibodies were present indicated as critical for eliminating the first infection and giving protection against subsequent viral challenges.This discovery suggests that antibody-mediated immunity is the most common way for people to respond to MERS-CoV. As a result, the decreased cells' antiviral actions may be critical during later phases of infection, particularly in terms tolerance to viral infection and viral survival The SARS-CoV virus activates and fortifies the immune system..Infection-related ARDS is characterized by an increase in cytokine production, an overabundance of immune cells, and uncontrolled epithelium destruction. (Yang et al., 2018). MERS-CoV can infect SARS-CoV was found in both CD4+ and CD8+ T cells isolated from human peripheral blood, tonsils, spleens, and lymphoid organs. This infection pattern might be attributed to decreased SARS-CoV receptor expression, namely ACE2 in T cells..Ying and colleagues (2016) Th1 type response appears to be crucial for SARS-CoV and MERS-CoV fulfillment control, and it is probable that this also applies to SARS-CoV-2 Patients infected with SARS-CoV-2 showed abnormally high levels of IL-1, IFN-, IP-10, and MCP-1., which are apparently the consequence of activated Th1 mobile responses (Huang et al., 2020). Unlike SARS-CoV infection, SARS-CoV-2 infection resulted in increased production of anti-inflammatory Th2 cytokines (e.g., IL-4 and IL-10) that inhibit inflammation, as opposed to SARS-CoV infection (Wong et al., 2004). Flow cytometric study of COVID-19 patients' PBMCs revealed a large contribution of CD4+ T cells that have been activated and CD14+ HLA-DRlo monocytes that produce granulocyte-macrophage colony-stimulating factor. (Zhou et al., 2020).Another take a look at recommended a drastically accelerated Polyclonal granulocyte-macrophage colony-stimulating factor+ polyclonal granulocyte-macrophage colony-stimulating factor+ polyclonal polyclonal polyclonal polyclonal poly In patients with immoderate IL-6 and IFN-production, CD4+ T cells can produce a large amount of IL-6 and IFN-ex vivo COVID-19 2020 (Zhou et al.). In the Xu et al. (Xu et al., 2020) observed an unusually significant number of CCR6+ Th17 cells in the peripheral blood of a patient with high COVID-19 levels, demonstrating the superiority of a Th17-type cytokine storm in this situation. Patients infected with MERS-CoV and SARS-CoV displayed enhanced Th17 responses or advanced IL-17-related pathways. (2013) (Josset and others) Lower IFN- and IFN-tiers with higher IL-17 exhibited a poorer very last outcome in MERS-CoV patients than the inverted phenotype (Faure et al, 2014). Furthermore, a study found that individuals With severe COVID-19, the number of regulatory T cells (Treg cells) was decreased (Qin et al., 2020). Because Treg cells have been identified proven in animal models to help in the resolution of ARDS inflammation (Walter et al., 2018), the absence of Treg cells may help ameliorate COVID-19 lung immunopathology. (Donget al., 2018). T cells are more active in mild COVID-19 and may be exhausted, as shown by non-forestalling. Inhibitory markers such PD-1 and T-cell immunoglobulin-3 are expressed, as is a general decrease in interest and cytotoxicity. In contrast, recovering patients had more follicular helper CD4+ T cells (TFH), lower levels of inhibitory markers, and higher amounts of effector molecules such as granzyme and perforin (Thevarajan et al ., 2020). Because the majority of the epitopes revealed for each virus are focused on viral structural proteins, matching the SARS-CoV/MERS-CoV epitopes with those connected to SARS-CoV-2 was achievable. SARS-CoV has been shown to contain lymphocytic epitopes for structural proteins including as S, N, M, and E proteins (Liu et al., 2017). Despite the fact that SARS-CoV ground proteins like as S, M, E, and N were all engaged in T-cell responses, with S protein accounting for the bulk of T-cell recognition epitopes. In people recovering with moderate COVID-19 (like to SARS-CoV-1 patients), strong T mobileular responses specific for viral N, M, and S proteins were slightly correlated with neutralizing antibody concentrations (Li et al., 2008). The identification of overlapping epitopes in many of the three viruses may assist in the creation of a cross-reactive vaccination that protects against all three. There will be various forms of human CoV in the future. Prompetchara and colleagues (2020). The cost and frequency of specific CD8+ memory T cells in SARS-CoV survivors exceeded that of CD4+ memory T cells, and virus-specific T cells survived for at least 6–11 years, indicating that T cells may also provide long-term protection (Tang et al., 2020). Virus-specific CD4+ and CD8+ T cells were identified at rates of 1.4 and 1.3 percent in all patients, respectively, and significantly reduced the frequency of CD4+ T-mobileular effector memory and effector memory RA cells. This research is excellent for using big complementary peptide pools including 1,1/2 of the SARS-CoV-2 epitopes. (Weiskopf et al., 2020). Rapid reduction in the price of lymphocytes in peripheral blood during the most severe stage of SARS-CoV infection (Li et al., 2004), T cells, in particular, are decreased, as are all T lymphocytes (CD4+ and CD8+) On the other hand, CD4+ T cells are more easily infected. CD4+ T cell depletion is associated with reduced lymphocyte recruitment, neutralizing antibody generation, and cytokine production in the lungs, As a consequence of the severe immune-mediated interstitial pneumonitis, but not with quicker SARS-CoV clearance from the lungs (Chen et al., 2010). Even the unusual alterations on the chest X-ray are preceded by lymphocyte depletion (Li et al., 2003). According to a During During a one-year follow-up of SARS patients, CD3+, CD4+, and CD8+ T cells unexpectedly returned sooner or later of the illness healing phase, and CD8+ T lymphocytes plummeted to daily internal 2–3 months after the illness began. Memory CD4+ T cells decline to every day one year after commencing, despite the fact that unique mobileular counts, which comprise fashionable T lymphocytes, CD3+ cells, CD4+ cells, and naïve CD4+ T cells, are lower than in healthy controls (Xie et al., 2006). Lympopenia appears to be caused by cytokines such as IFN-I and TNF-a, which can also inhibit T-mobileular recirculation in blood by promoting lymphoid organ retention and endothelial attachment (Kamphuis et al., 2006), or endogenous or exogenous glucocorticoids, which induce lymphocyte apoptosis in the long run (Panesar,2006; Panesar, 2008).

Materials and Methods

Specimens Collection

The study was performed using (180) of blood specimens. They were collected from Hospital in Baghdad Medical City according to the research ethics form and The practical laboratory work was accomplished in private research laboratories. The specimens were taken from patients of different ages with covid-19 . Specimens of blood was taken and obtained from each patient via vein puncture method. These specimens were divided into three groups as follows:

Moderate group,Sever group,Critical group

3ml of blood was taken from patients and placed into gel tubes and allowed to clot for ~30 minutes .Separation of serum into plain tubes and stored in deep freeze .The study was done in the private research laboratories .

 : Kits used in this study with origin

CD4 ELISA Kit (H CUSABIO{U5A})

CD8 ELISA Kit (H CUSABIO{U5A})

ELISA Assay

The "Enzyme linked immunosorbent assay" (ELISA) was used to identify both CD4 and CD8 of covid-19 in serum samples.

RESULT AND DISCUSSION

Detection of covid-19 infection:

Using the PCR technique to detect covid-19 infection in the investigated samples, 158 patients were found to be positive for the virus, whereas 22 were found to be negative (control group)as displayed in the table (1).

Table 1: Distribution the sample study according to results of patients Group

Group	No	Percentage (%)
Critical	56	35.44
Severe	78	49.37
Moderate	24	15.19
Total	158	100%
P - value	----	0.0002 **
** (P ≤ 0.01).		

As shown in the table (1), the study categorize patients in relation to the severity into 4 groups .the sever high percentage 49.37% than critical 35.44% and moderate 15.19 % were chosen randomly as a study group with a high significant different ($p < 0.01$).

Table 2: In CD4 and CD8, there is a comparison between different groupings. conc.

Group	Mean ± SE	
	CD4 conc.	CD8 conc.
Critical	4.76 ±0.14 b	880.19 ±52.03 a
Severe	5.68 ±0.16 a	961.74 ±49.48 a
Moderate	3.83 ±0.09 c	647.52 ±44.54 b
Control	3.71 ±0.07 c	384.02 ±26.09 c
LSD value	0.544 **	178.53 **
P-value	0.0001	0.0001

Means in the same column with different letters differed considerably. ** (P≤0.01).

As shone in table 2 in our study the concentration of CD4 and CD8 high in sever (CD4 5.68 ±0.16-CD8 961.74 ±49.48) than critical (CD4 4.76 ±0.14- CD8 880.19 ±52.03)and moderate (CD43.83 ±0.09 – CD8 647.52 ±44.54) groups with high significant different (P≤0.01) but it's been stated CD4+ T cells and CD8+ T cells were shown to be reduced more in the worst cases of COVID-19 than in the mild cases (Nishiga et al., 2020;Liu et al., 2020; Ni et al., 2020).

REFERENCES

1. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. J Med Virol (2020) 92:418–423.

2. ZhuN,ZhangD,WangW,LiX,YangB,SongJ,ZhaoX,HuangB,ShiW,LuR,etal. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med (2020) 382:727–733. doi:10.1056/NEJMoa2001017

3. WuF,ZhaoS,YuB,ChenYM,WangW,SongZG,HuY,TaoZW,TianJH,PeiYY,et al. A new coronavirus associated with human respiratory disease in China. Nature (2020) 579:265–269. doi:10.1038/s41586-020-2008-3

4. Naming the coronavirus disease (COVID-19) and the virus that causes it. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical- guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it [Accessed June 8, 2020]

5. Helmy YA, Fawzy M, Elaswad A, Sobieh A, Kenney SP, Shehata AA. The COVID-19 Pandemic : A Comprehensive Review of Taxonomy , Genetics , Epidemiology , Diagnosis , Treatment , and Control. J Clin Med (2020) 9:1–29.

6. Xiao Z, Xie X, Guo W, Luo Z, Liao J, Wen F, Zhou Q, Han L, Zheng T. Examining the incubation period distributions of COVID-19 on Chinese patients with different travel histories. J Infect Dev Ctries (2020) 14:323–327. doi:10.3855/jidc.12718

7. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, Azman AS, Reich NG, Lessler J. The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. Ann Intern Med (2020) 172:577– 582. doi:10.7326/M20-0504

8. Xiao Z, Xie X, Guo W, Luo Z, Liao J, Wen F, Zhou Q, Han L, Zheng T. Examining the incubation period distributions of COVID-19 on Chinese patients with different travel histories. J Infect Dev Ctries (2020) 14:323–327. doi:10.3855/jidc.12718

9. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, Yang J, Xing F, Liu J, Yip CCY, Poon RWS, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet (2020) 395:514–523. doi:10.1016/S0140-6736(20)30154-9

10. Khedmat L. New Coronavirus (2019-nCoV): An Insight Toward Preventive Actions and Natural Medicine. IJTMGH (2020) 8:44–45. doi:10.34172/ijtmgh.2020.07

11. Raghad G. Ali Al-Suhail, Layla Fouad Ali.2020. Statistical Analysis of COVID-19 Pandemic Across the Provinces of Iraq. Iraqi Journal of Science, 2021, Vol. 62, No. 3, pp: 811-824. DOI: 10.24996/ijs.2021.62.3.12. ISSN: 0067-2904.

12. OCHA. IRAQ : COVID-19. (2020).

13. OCHA. IRAQ : COVID-19. (2020).

14. OCHA. IRAQ : COVID-19. (2020).

15. OCHA. IRAQ : COVID-19. (2020).

16. Zhu, N. et al., 2020. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 382, 727-733.

17. Fehr, A.R. & Perlman, S. 2015. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol 1282, 1-23.

18. Zhou, P. et al., 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270-273.

19. Rogers MC, Williams JV. Quis custodiet ipsos custodes? regulation of cell-mediated immune responses following viral lung infections. Annu Rev Virol. 2018 Sep 29;5(1):363–83.

20. Yang CY, Chen CS, Yiang GT, Cheng YL, Yong SB, Wu MY, et al. New insights into the immune molecular regulation of the pathogenesis of acute respiratory distress syndrome. Int J Mol Sci. 2018 Feb 16;19(2):588.

21. 202-Ying T, Li W, Dimitrov DS. Discovery of T-cell infection and apoptosis by middle east respiratory syndrome coronavirus. J Infect Dis. 2016 Mar 15;213(6):877–9.

22. Wong CK, Lam CW, Wu AK, Ip WK, Lee NL, Chan IH, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin Exp Immunol. 2004 Apr;136(1):95–103

23. Zhou Y, Fu B, Zheng X, Wang D, Zhao C, Qi Y, et al. Aberrant pathogenic GM-CSF+ T cells and inflammatory CD14+CD16+ monocytes in severe pulmonary syndrome patients of a new coronavirus. bioRxiv. 2020.

24. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020 Apr;8(4):420–2.

25. Josset L, Menachery VD, Gralinski LE, Agnihothram S, Sova P, Carter VS, et al. Cell host response to infection with novel human coronavirus EMC predicts potential antivirals and important differences with SARS coronavirus. mBio. 2013 Apr 30;4(3):e00165–13.

26. Faure E, Poissy J, Goffard A, Fournier C, Kipnis E, Titecat M, et al. Distinct immune response in two MERS-CoV-infected patients: can we go from bench to bedside? PLoS One. 2014;9(2):e88716.

27. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020;71(15):762–8.

28. Walter JM, Helmin KA, Abdala-Valencia H, Wunderink RG, Singer BD. Multidimensional assessment of alveolar T cells in critically ill patients. JCI Insight. 2018;3(17):e123287.

29. Dong P, Ju X, Yan Y, Zhang S, Cai M, Wang H, et al. γδ T cells provide protective function in highly pathogenic avian H5N1 influenza A virus infection. Front Immunol. 2018;9:2812.

30. Thevarajan I, Nguyen THO, Koutsakos M, Druce J, Caly L, van de Sandt CE, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nat Med. 2020 Apr 1;26(4):453–5.

31. Liu WJ, Zhao M, Liu K, Xu K, Wong G, Tan W, et al. T-cell immunity of SARS-CoV: implications for vaccine development against MERS-CoV. Antiviral Res. 2017 Jan;137:82–92.

32. Prompetchara E, Ketloy C, Palaga T. Immune responses in COVID-19 and potential vaccines: lessons learned from SARS and MERS epidemic. Asian Pac J Allergy Immunol. 2020 Mar;38(1):1–9.

33. Li CK, Wu H, Yan H, Ma S, Wang L, Zhang M, et al. T cell responses to whole SARS coronavirus in humans. J Immunol. 2008 Oct 15;181(8):5490–500.

34. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020 Apr;18(4):844–7.

35. Weiskopf D, Schmitz KS, Raadsen MP, Grifoni A, Okba NMA, Endeman H, et al. Phenotype and kinetics of SARS-CoV-2-specific T cells in COVID-19 patients with acute respiratory distress syndrome. Sci Immunol. 2020 Jun 26;5(48):5.

36. Li T, Qiu Z, Zhang L, Han Y, He W, Liu Z, et al. Significant changes of peripheral T lymphocyte subsets in patients with severe acute respiratory syndrome. J Infect Dis. 2004 Feb 15;189(4):648–51.

37. Chen J, Lau YF, Lamirande EW, Paddock CD, Bartlett JH, Zaki SR, et al. Cellular immune responses to severe acute respiratory syndrome coronavirus (SARS-CoV) infection in senescent BALB/c mice: CD4+ T cells are important in control of SARS-CoV infection. J Virol. 2010;84(3):1289–301.

38. Li T, Qiu Z, Han Y, Wang Z, Fan H, Lu W, et al. Rapid loss of both CD4+ and CD8+ T lymphocyte subsets during the acute phase of severe acute

respiratory syndrome. Chin Med J. 2003 Jul;116(7):985–7.

39. Xie J, Fan HW, Li TS, Qiu ZF, Han Y. [Dynamic changes of T lymphocyte subsets in the long-term follow-up of severe acute respiratory syndrome patients]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2006 Apr;28(2):253–5.

40. Kamphuis E, Junt T, Waibler Z, Forster R, Kalinke U. Type I interferons directly regulate lymphocyte recirculation and cause transient blood lymphopenia. Blood. 2006;108(10):3253–61.

41. Panesar NS. Glucocorticoid treatment of patients with SARS: implications for mechanisms of immunopathology. Nat Rev Immunol. 2006;6(4):334.

42. Panesar NS. What caused lymphopenia in SARS and how reliable is the lymphokine status in glucocorticoid-treated patients? Med Hypotheses. 2008 Aug;71(2):298–301.

43. Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nat Rev Cardiol. (2020)

44. Liu J, Li S, Liang B, Wang X, Wang H, Li W, et al. . Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMed. (2020)

45. Ni M, Tian FB, Xiang DD, Yu B. Characteristics of inflammatory factors and lymphocyte subsets in patients with severe COVID-19. J Med Virol. (2020)