ISSN: 2588-4115; Infection Epidemiology and Microbiology. 2024;10(4):329-333 doi 10.52547/iem.10.4.329

Serum Level of Some Immunological Markers in COVID-19 Patients in Diyala Province, Iraq

ARTICLE INFO

Article Type
Original Article

Authors
Shahrazad Ahmed Khalaf, *PhD*[1*]

Department of Biotechnology, College of Science, Diyala University, Diyala, Iraq.

** Correspondence*
Department of Biotechnology, College of Science, Diyala University, Diyala, Iraq.
E-mail: ShahrazadAh.Kh@uodiyala.edu.iq

How to cite this article
Khalaf Sh.A. Serum Level of Some Immunological Markers in COVID-19 Patients in Diyala Province, Iraq. Infection Epidemiology and Microbiology. 2024;10(4): 329-333.

Article History
Received: July 08, 2024
Accepted: October 12, 2024
Published: December 20, 2024

ABSTRACT

Background: This study aimed to measure the levels of IL1-β, IL18-, and IFN-Y in the sera of patients with severe COVID-19 in Diyala province in Iraq..
Materials & Methods: Blood samples were collected from 60 patients in Baquba Teaching Hospital in Iraq between January and April 2021, these patients had clinical signs and symptoms of COVID-19, diagnosed by the hospital doctors; in addition, 30 samples were taken from healthy control people, and the levels of IL-1β, IL-18, and IFN-Y markers were detected in COVID-19 patients and the control group by ELISA (enzyme-linked immunosorbent assay) technique.
Findings: This study displayed the high level of IL-1β, IL-18, and IFN-Y in COVID-19 patients compared with the control group (154.04 ± 16.54 versus 85.41 ± 8.9 pg/mL, 82.88 ± 7.96 versus 66.67 ± 9.34 pg/mL, and 116.06 ± 26.5 versus 97.96 ± 12.2pg/mL, respectively). This study also showed a high prevalence of COVID-19 in males compared to females. In the sera of COVID-19 patients, the levels of IL-1β, IL-18, and IFN-Y were noticeably higher in females than in males.
Conclusion: There was a significant difference in the levels of IL-1β, IL-18, and IFN-Y between the study groups; also, they were higher in females than in males.

Keywords: COVID-19 patient, IL-1β, IL-18, IFN-Y.

CITATION LINKS

[1] Iwamura AP, et al. Immunity and inflammatory... [2] Zhu N,et al. A novel coronavirus from patients... [3] Yang X, et al. Clinical course and outcomes... [4] De Jesus AA, Molecular mechanisms in... [5] Lu Q, et al. Discussion about clinical value of... [6] Chousterman BG, Cytokine storm and sepsis disease... [7] Huang C, et al. Clinical features of patients infected... [8] Xu Z, et al. Pathological findings of COVID-19... [9] Yang X, et al. Naturally activated adaptive immunity... [10] Dinarello CA. The IL-1 family of cytokines... [11] Orzalli MH, An antiviral branch of the IL-1... [12] Jamilloux Y, et al. Should we stimulate or suppress immune... [13] Martinon F, The inflammasome: A molecular platform... [14] Mardi A, Interleukin-1 in COVID-19 infection... [15] Shimizu M. Clinical features of cytokine... [16] Arend WP, Palmer G, Gabay C. IL-1, IL-18, and... [17] Flament H, et al. Outcome of SARS-CoV-2 infection is... [18] Zhao J, et al. Airway memory CD4+ T cells mediate... [19] Shirley R. Development of targeted gene... [20] Madfoon ZM, Comparison of some immunological ... [21] Zhao Y, et al. Longitudinal COVID-19 profiling... [22] Mulchandani R, Deciphering the COVID-19 cytokine...

Introduction

SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2) is the cause of the clinical infection identified as coronavirus disease 2019 (COVID-19). Patients may be asymptomatic, exhibit respiratory and digestive symptoms, or even experience multiple organ failure, which could be fatal [1]. The first event of SARS-CoV-2 infection was described in Wuhan, China in December 2019. The newly discovered illness, known as COVID19-, continues to pose a serious danger to public health on a global scale [2]. Asymptomatic patients are likely to spread the extremely infectious SARS-CoV-2 [3]. The primary determinant of COVID19-progression severity is the delicate balance between an efficient antiviral response and deregulated immunological responses [1]. In addition to being involved in several pathophysiological processes necessary for survival, such as inflammation, tissue healing, fibrosis, and coagulation, cytokines are crucial for the immune system's effective functioning. However, when the immune system doesn't work properly, cytokines could be produced in excess, which is harmful to the body, this state is called a cytokine storm, which causes systemic hyperinflammation [4]. In critically-ill and severe patients, inflammatory markers are frequently elevated [5], including IL-1, CSF, chemokine, IFN, TNF, chemokine, and GF [6, 7]. Previous studies have documented that COVID-19 patients experience significant conditions related to lymphopenia and increased proinflammatory cytokines [8]. Immune cells respond to COVID-19 infection by modifications in T and B cell populations in COVID-19 patients, which help elucidate the immune response to this infection and provide insights for diagnosis and therapy. T and B cells are critical for defense against viral infections and response to infections [9]. Therefore, the current study aimed to evaluate the levels of IL-1β, IL-18, and IFN-Ɣ in patients with COVID-19 infection.

Objectives: To detect the effect of some immunological parameters and their association with the COVID-19 disease, the level of IL-1β, IL-18, and IFN-Ɣ in patients was measured.

Materials and Methods

This study was conducted in Baquba Teaching Hospital between January and April 2021. A total of 60 blood samples (32 males and 28 females) from COVID-19 patients and 30 blood samples (16 males and 14 females) from healthy control people were collected. Patients with previous respiratory infection or chronic inflammation and smokers were excluded from the current study. After 12 hours of fasting, blood samples were taken from venous blood and centrifuged at 4000 rpm for 10 minutes for virus detection using the COVID-19 strip kit from BioMérieux. The levels of IL-1β, IL-18, and IFN-γ in the sera of patients were detected by ELISA (enzyme-linked immunosorbent assay) using test kits from Sunlong Human Diagnostics Company.

Statistical analysis: Statistical analysis was performed by t-test through IBM SPSS statistical software Version 21.

Findings

A total of 90 blood samples were collected: 60 (66.6%) samples from COVID-19 patients and 30 (33.3%) samples from healthy controls. Among COVID-19 patients, 32 (35.5%) patients were male, while 28 (31.1%) patients were female as shown in (Table 1).

A higher level of IL-1β was found in COVID-19 patients compared with the control group (154.04 ± 16.54 versus 85.41 ± 8.9 pg/mL), and this difference between the two groups was highly significant ($p< 0.05$) as shown in Table 2. In the current research, the prevalence of IL-1β level in COVID-19

Table 1) Frequency spreading of the study groups by gender

Parameter		Study Groups [Mean ± SD]		*P* Value
IL-1 β	Patient vs Control	154.04 ± 16.54	85.41 ± 8.9	<0.05
	Female vs male	167.26 ± 8.94	142.38 ± 12.37	<0.05
IL-18	Patient vs Control	82.88 ± 7.96	66.67 ± 9.34	< 0.05
	Female vs male	88.68 ±4.28	76.03 ± 5.28	<0.05
IFN-Ɣ	Patient vs Control	116.06 ± 26.5	97.96 ± 12.2	< 0.05
	Female vs male	126.93 ± 21.76	103.64 ± 26.32	<0.05

Table 2) Comparison of IL-1β, IL-18, and IFN-Ɣ levels between Study groups

Study group	Male		Female		Total (n=90)	
	No.	%	No.	%	No.	%
Patient	32	35.5	28	31.1	60	66.6
Control	16	17.7	14	15.5	30	33.3

patients was higher among females tha males as shown in Table (2). The mean concentration of IL-1β level was 167.26 ± 8.94 (SD) pg/mL in female patients and 142.38 ± 12.37 pg/mL in male patients. The results showed that this difference between female and male patients was significant. A higher level of IL-18 was found in COVID-19 patients compared with the control group (82.88 ± 7.96 versus 66.67 ± 9.34 pg/mL), and this difference between the two groups was significant ($p< 0.05$) as shown in Table 2. In the current research, the incidence of IL-18 level in COVID-19 was higher among females than among males as shown in (Table2). The mean concentration of IL-18 level was 88.68 ±4.28 pg/mL in female patients and 76.03 ± 5.28 pg/mL in male patients. The results showed that there was a significant difference between female and male patients in this regard. A higher level of IFN-Ɣ was found in COVID-19 patients compared with a control group (116.06 ± 26.5 versus 97.96 ± 12.2pg/mL), and this difference between the two groups was significant ($p< 0.05$) as shown in Table 2. In the current research, the incidence of IFN-Ɣ level in COVID-19 was higher among females than among males as shown in (Table2). The mean concentration of IFN-Ɣ level was 126.93 ± 21.76 pg/mL in female patients and 103.64 ± 26.32 pg/mL in male patients.

The results showed that there was a significant difference between male and female patients in this regard ($p< 0.05$).

Discussion

IL-1 is an essential cytokine involved in inducing inflammation [10]. IL-1 has a strong antiviral action and supports the immune system's ability to combat viral infection [11]. In patients with pneumonia caused by COVID-19, IL1- is found in peripheral blood and bronchial lavage fluid (BALF) [12]. IL-1 is activated and released after the initiation of inflammation [13]. Numerous previous studies have discovered that IL-1β levels increase through COVID-19 infection [14]. Due to uncontrollable high immune responses during COVID-19 infection, the IL-1 cytokine is of critical importance in initiating the cytokine storm [14].

IL-1 is released from macrophages, mast cells, endothelium, and epithelial cells, a significant proinflammatory cytokine of the innate immune response [15]. Cytokine storm is caused by a sudden and sharp increase in

the many proinflammatory cytokines levels in the blood, for example INF, IL-1, and TNF-α. The increase in cytokines causes a variety of immune cells such as neutrophils and macrophages to swarm into the infection site from the circulation. Among the disastrous effects that this condition could have on human tissue are intercellular endothelial breakdown, vascular barrier destruction, capillary damage, and finally death. cytokine storm could lead to lung damage and progress into acute lung injury [15]. IL-18 is involved in fibrosis and hematopoiesis and plays an significant role in nonspecific and specific immune responses [16]. Increased IL-18 levels and activation of mucosal-associated invariant T [MAIT] cells have been documented in the lungs and blood of COVID19- patients [17], these cells are innate-like T cells implicated in mucosal viral defenses, which use the IL--18IFN-a axis to exhibit a strong cytotoxic phenotype in the lungs [18].

The high production rate of interferon-gamma (IFN-γ) shows that the immune system is preventing the infection caused by the COVID-19 virus [18]. The improved synthesis of ACE2 (angiotensin-converting enzyme 2), which serves as a key to virus entrance into cells, is stimulated by IFN secreted by T-helper cells. This allows the virus to proliferate indefinitely and decreases the cell's resistance to the virus [19]. IFN is an anti-inflammatory cytokine that rises in the last phases of infection; hence, its increase is related to the end of the infection phase [20]. The present study is in line with previous studies [21]. Several studies have shown that interferon-gamma levels are higher in patients with COVID-19 compared with healthy people [1, 7, 21], and these results are consistent with the results of the current study. Plasma cytokine levels in 41 COVID-19 confirmed cases were examined in a study in China, and it was found that both IFN-γ and IL-1β were elevated in patients admitted to the intensive care unit and in non-ICU patients compared to healthy people. Six of the study participants passed away from pneumonia, and 33% of the patients required ICU admission [7]. Reduced T cells and noticeably elevated pro-inflammatory cytokine levels are hallmarks of severe COVID-19 [22].

Study limitations: The seriousness of the infection and the speed of its transmission are the most important limitations of this study.

Conclusion

There were significant alterations in the percentage of IL-1β, IL-18, and IFN-Ɣ between the study groups; also, their levels were higher in females than in males.

Acknowledgments

The author would like to thank Baquba Teaching Hospital for providing them with samples.

Authors' contributions: The author worked to collect samples, analyze them, and write up the results and research.

Fundings: Not applicable.

Conflicts of interest: The author declare no conflict of interest.

Ethical approval: No ethics were established for the research because the research was conducted under the supervision of physician in a government hospital and all samples were taken from the laboratory in the hospital patients' diagnostic stages, and no additional samples were taken.

Consent to participate: This section does not apply to this article because it was completely a laboratory study and no patient or participant was included in it.

References

1. Iwamura AP, Tavares da Silva MR, Hümmelgen AL, Soeiro Pereira PV, Falcai A, Grumach AS, et al. Immunity and inflammatory biomarkers in

COVID-19: A systematic review. Rev Med Virol. 2021;31(4):e2199.
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33.
3. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81.
4. de Jesus AA, Canna SW, Liu Y, Goldbach-Mansky R. Molecular mechanisms in genetically defined autoinflammatory diseases: Disorders of amplified danger signaling. Ann Rev Immunol. 2015;33(1):823-74.
5. Lu Q, Zhu Z, Zhou H, Hu Y, Shen G, Zhu P, et al. Discussion about clinical value of detection of IL-10, IL-1β, IL-6, MCP-1, TNF-α, IP-10, and IL-4 for the diagnosis of COVID-19. Authorea. 2020.
6. Chousterman BG, Swirski FK, Weber GF. Cytokine storm and sepsis disease pathogenesis. Semin Immunopathol.2017;39:517-28.
7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
8. 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;8(4):420-2.
9. Yang X, Dai T, Zhou X, Qian H, Guo R, Lei L, et al. Naturally activated adaptive immunity in COVID-19 patients. J Cell Mol Med. 2020;24(21):12457-63.
10.Dinarello CA. The IL-1 family of cytokines and receptors in rheumatic diseases. Nat Rev Rheumatol.2019;15(10):612-32.
11. Orzalli MH, Smith A, Jurado KA, Iwasaki A, Garlick JA, Kagan JC. An antiviral branch of the IL-1 signaling pathway restricts immune-evasive virus replication. Mol Cell. 2018;71(5):825-40.
12. Jamilloux Y, Henry T, Belot A, Viel S, Fauter M, El Jammal T, et al. Should we stimulate or suppress immune responses in COVID-19? Cytokine and anti-cytokine interventions. Autoimmun Rev. 2020;19(7):102567.
13. Martinon F, Burns K, Tschopp J. The inflammasome: A molecular platform triggering activation of inflammatory caspases and processing of proIL-β. Mol Cell. 2002;10(2):417-26.
14. Mardi A, Meidaninikjeh S, Nikfarjam S, Majidi Zolbanin N, Jafari R. Interleukin-1 in COVID-19 infection: Immunopathogenesis and possible therapeutic perspective. Viral Immunol. 2021;34(10):679-88.
15. Shimizu M. Clinical features of cytokine storm syndrome. In: Cron R, Behrens E, editors. Cytokine storm syndrome. Springer, Cham; 2019, p. 31-41.
16. Arend WP, Palmer G, Gabay C. IL-1, IL-18, and IL-33 families of cytokines. Immunol Rev. 2008;223(1):20-38.
17. Flament H, Rouland M, Beaudoin L, Toubal A, Bertrand L, Lebourgeois S, et al. Outcome of SARS-CoV-2 infection is linked to MAIT cell activation and cytotoxicity. Nat Immunol. 2021;22(3):322-35.
18. Zhao J, Zhao J, Mangalam AK, Channappanavar R, Fett C, Meyerholz DK, et al. Airway memory CD4+ T cells mediate protective immunity against emerging respiratory coronaviruses. Immunity. 2016;44(6):1379-91.
19. Shirley R. Development of targeted gene delivery vectors to assess cardiac overexpression of ACE2 in vivo (doctoral dissertation). University of Glasgow; 2008.
20.Madfoon ZM, Mezher MN, Mohammed S. Comparison of some immunological parameters of COVID-19 patients with and without diabetes according to age groups and gender. Pakistan J Med Health Sci. 2022;16(03):476-8.
21. Zhao Y, Qin L, Zhang P, Li K, Liang L, Sun J, et al. Longitudinal COVID-19 profiling associates IL-1RA and IL-10 with disease severity and RANTES with mild disease. JCI Insight. 2020;5(13):e139834.
22. Mulchandani R, Lyngdoh T, Kakkar AK. Deciphering the COVID-19 cytokine storm: Systematic review and meta-analysis. Eur J Clin Invest. 2021;51(1):e13429.