IL-6, IL-0, IFN Gamma and CRP in Newly Diagnosed COVID 19 Patients

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Abstract

The study was conducted in Baghdad for the period from July 1 to August 20 2020 on patients previously diagnosed with the emerging corona virus .. The study included 40 patients whose ages ranged from 20 to 80 years. The study also included taking 40 healthy people of the same age groups to detect interleukin 6 and 10 gamma interferon by using ELISA technique as well as measuring the level of the C-reactive protein. The study contained a withdrawal of five ml of venous blood from patients and patients and took all the necessary information from them such as gender, age, current living status, number of family members, as well as the history of infection and travel to countries affected by the virus to compare the two groups with regard to the immune response by measuring the variables above. The study showed that the highest mean level of IL-6 was found in newly diagnosed COVID-19 patients comparing with healthy control (60.76±8.46 *v.s.*39.03±5.26 pg/ml) (P:<0.01). The study also demonstrated that the level of IL-10 was significantly elevated in newly diagnosed COVID-19 patients as compared with healthy control (38.18±4.57 *v.s.*31.84±3.19 pg/ml). The study established that the level of IFN-Gamma was significantly increased in patients with new infection of COVID-19 as compared with healthy control (27.27±7.18 *v.s.* 13.81±3.83 pg/ml) (P:<0.01). The study proven that the level of CRP was increased significantly in patients with new infection of COVID-19 as compared with healthy control (33.18±3.19 *v.s.*3.±1.81 mg/dl) (P:<0.01). The study concluded that, There was a highly significant relation of IL-6, IL-0, IFN gamma, and CRP with COVID-19 disease in the first week of infection

Keyword: *COVID-19; SARS COV2; IL-6; IFN gamma; CRP.*

Introduction

The presence of a new virus belonging to the Coronavirus family was announced at the end of 2019 in Wuhan, China, and it was recently agreed to name it as Covid-19, SARS-Coronavirus2[(1)]. It was declared by the World Health Organization (WHO) as an epidemic that spread rapidly around the world and raised international concern and raised the state of emergency in all countries that it entered due to its rapid spread and the lack of clarity of all signs of infection as it is a new virus that infects humans and is transmitted from animals and then transmitted between humans and humans [(2)]. The genetic sequence of the virus represents a 96% and 79.5% match for the bat coronavirus and SARS-CoV, respectively. Such as SARS-CoV and MERS-CoV. The previous evidence also showed that most patients have shown that the level of cytokines and immune proteins are among the most important causes of patients 'recovery first, and then it is possible that these cytokines will do the opposite in the deterioration of the disease by forming the so-called cytokines storm[(3,4)]. However, until this moment, there are scarce studies about what the virus is and the true immune role of the host's body towards the

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virus, especially as it was presented that the virus is new and information about its pathogenicity is not available in an accurate and clear way[5]. Studies indicate that the COVID-19 virus was more likely to affect adults of older ages and the elderly who have associated diseases such as diabetes, high weakness, heart and lung problems, and whose immunity is low due to the presence of those diseases that are characterized by low immunity [6, 7]. Especially since the virus is a virus with a new strain that has not yet been known about the true condition of the infected, the high rates of infection and the spread of disease among groups of society and the elderly in particular, and that the high levels of inflammatory cytokines among people with the good coronavirus and not many people know about the nature of the immune response for patients infected with the emerging coronavirus[8]. So the aim of the study was to estimate the level of IL-6, IL-0, IFN gamma and CRP in patients with COVID-19 infection.

Material and Method

The study was conducted in Baghdad for the period from July 1 to August 20 2020 on patients previously diagnosed with the emerging corona virus .. The study included 40 patients whose ages ranged from 20 to 80 years. The study also included taking 40 healthy people of the same age groups to detect interleukin 6 and 10 gamma interferon by using ELISA technique (Koma biotech, ELISA, USA).as well as measuring the level of the C-reactive protein. The study contained a withdrawal of five ml of venous blood from patients and patients and took all the necessary information from them such as gender, age, current living status, number of family members, as well as the history of infection and travel to countries affected by the virus to compare the two groups with regard to the immune response by measuring the variables above.

Findings: As shown in Table 1. There was no significant difference between studied cases and the control group regarding patient age.

Table 1: Clinical characteristics of studied women

Parameters (Mean±SD)	Pregnant women	Control group
No.	40	40
Age (yeas)	52.1±6.7	50.6±5.6
Sex	35 male, 15 female	33 male, 17 female
Mean 24 h SBP, mm Hg	128.7±11.5 *	110.8±7.4
Mean 24 h DBP, mm Hg	83.5±6.9*	69.4±8.3
Maximal SBP, mm Hg	167±24.1*	119.0±10.2
Maximal DBP, mm Hg	109.1±22.7*	74.7±13.3

The study showed that the highest mean level of IL-6was found in newly diagnosed COVID-19 patients comparing with healthy control (60.76±8.46*v.s.*39.03±5.26 pg/ml) (P:<0.01).

Table 2: Levels of IL-6 in newly diagnosed COVID-19 patients and the control group

Group	Mean (pg/ml)	SD	P value
COVID-19 patients	60.76	8.46	<0.05
Healthy group	39.03	5.26	

The study also demonstrated that the level of IL-10 was significantly elevated in newly diagnosed COVID-19 patients as compared with healthy control (38.18±4.57 *v.s.*31.84±3.19 pg/ml) (P:<0.01), Table 3.

Table 3: Levels of IL-10 in newly diagnosed COVID-19 patients and the control group

Group	IL-10 Mean (pg/ml)	SD	P value
COVID-19 patients	38.18	4.57	<0.05
Healthy group	31.84	3.19	

The study established that the level of IFN-Gamma was significantly increased in patients with new infection of COVID-19 as compared with healthy control (27.27±7.18 *v.s.*13.81±3.83 pg/ml) (P:<0.01), Table 4.

Table 4: Levels of IFN-Gamma in newly diagnosed COVID-19 patients and the control group

Group	IFN-Gamma Mean (pg/ml)	SD	P value
COVID-19 patients	27.27	7.18	<0.05
Healthy group	13.81	3.83	

The study proven that the level of CRP was increased significantly in patients with new infection of COVID-19 as compared with healthy control (33.18±3.19 *v.s.*3.±1.81 mg/dl) (P:<0.01), Table 5.

Table 4: Levels of CRPin newly diagnosed COVID-19 patients and the control group

Group	CRP Mean (mg/dl)	SD	P value
COVID-19 patients	33.18	3.19	<0.05
Healthy group	4.17	1.81	

Table 5: Correlation of CRP with each parameter in the study

Parameter	R value
IL-6	0.7
IL-10	0.52
IFN-Gamma	0.49

Discussion

In this study, levels of IL-6, IL-0, IFN gamma, and CRP were increased in subjects with coronavirus, and I mean Yen, who was newly diagnosed with the virus by nasopharyngeal swab examination and polymerase chain reaction method. It should be noted that the observed increase in the levels of g variables. Several very recent global responses indicate that IFNγ and IL-6 F levels are positively associated with an increased infection with the Covid 19 virus that causes acute respiratory syndrome (9). Other studies suggest that an excess of these cytokines and other inflammatory agents may cause the body to create a so-called cytokine storm (10, 11). While this virus multiplies in the cells of the upper respiratory system and then descends gradually until it reaches the internal lung tissues, the increase in the secretions of cytokines above may lead to acute respiratory distress syndrome associated with the new corona virus as a result of bulimia and acute reproduction. From a virus with induction of conventional antiviral immunity and with a crisis associated with a possible peak phase of T cell responses. However, it is not clear whether immune hyperactivity or failure to resolve the inflammatory response due to persistent viral replication or immune dysregulation underlies severe disease (12). Several recent responses undertaken to determine the role of immunity and the immune response to Covid-19 indicate that interleukin-6 and CRP are elevated in patients with COVID-19, particularly those with comorbidities such as diabetes and chest and vascular pain (13-16). Other studies have also indicated two settings induced by viral infection and epithelial cell proliferation in the airway in high levels of viral-associated acid inflammation with associated vascular leakage, as seen in SARS-CoV53 patients. Prostatitis is a highly inflammatory form of programmed cell death that is commonly observed with cytokine viruses 54. This is a potential trigger for a subsequent inflammatory response (17, 18). It is worth noting that another study conducted in advance during the past few months reported that the highest levels of serum inflammatory cytokines, interleukin-6 and CRP were in patients diagnosed with severe Covid-19 compared to individuals with mild disease, similar to the

results of our study that confirmed this, which stated that There was a significant positive correlation of CRP with all cytokines that were taken in the current study (19). Some scientists believe that the rise of these pathogens, in addition to other factors that have not been taken into account, may play a vital role in the fluctuation of autoimmunity first, then the original immunity in patients infected with the new coronavirus, Covid 19 (20). Although there was no direct evidence that cytokines and inflammatory chemicals were involved in lung disease during COVID-19, changes in laboratory parameters, including elevated blood cytokines, chemokine levels, and increased CRP in affected patients, were associated with disease severity and adverse outcomes(21).

Conclusions

Levels of IL-6, IL-0, IFN gamma, and CRPwere elevated significantly in patients with COVID-19 disease in the first week of infection

Conflict of Interest: None

Source of Findings: None

Ethical Clearance: None

References

1. 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 1;38(1):1-9.
2. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K, Antoniadou A, Antonakos N, Damoraki G, Gkavogianni T, Adami ME, Katsaounou P, Ntaganou M. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. Cell host & microbe. 2020 Apr 21.
3. Weitz JS, Beckett SJ, Coenen AR, Demory D, Dominguez-Mirazo M, Dushoff J, Leung CY, Li G, Măgălie A, Park SW, Rodriguez-Gonzalez R. Modeling shield immunity to reduce COVID-19 epidemic spread. Nature medicine. 2020 May 7:1-6.
4. Azkur AK, Akdis M, Azkur D, Sokolowska M, van de Veen W, Brüggen MC, O'Mahony L, Gao Y, Nadeau K, Akdis CA. Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. Allergy. 2020 Jul; 75(7):1564-81.
5. Yang Y, Lu Q, Liu M, et al. Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China. 2020. 2020.02.10.20021675.
6. Wong CK, Lam CW, Wu AK, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin Exp Immunol 2004; 136:95–103.
7. Mahallawi WH, Khabour OF, Zhang Q, Makhdoum HM, Suliman BA. MERS-CoV infection in humans is associated with a pro-inflammatory Th1 and Th17 cytokine profile. Cytokine 2018; 104:8–13.
8. National Health Commission of the Peoples Republic of China. The Fifth Revised Trial Version of the Novel Coronavirus Pneumonia Diagnosis and Treatment Guidance. Available at: http://www.nhc.gov.cn/yzygj/s7652m/202002/41c3142b38b84ec4a748e60773cf9d4f.shtml.
9. Google Scholar
10. Luo Y, Xie Y, Zhang W, et al. Combination of lymphocyte number and function in evaluating host immunity. Aging (Albany NY) 2019; 11:12685–707.
11. Hou H, Zhou Y, Yu J, et al. Establishment of the reference intervals of lymphocyte function in healthy adults based on IFN-γ secretion assay upon phorbol-12-myristate-13-acetate/ionomycin stimulation. Front Immunol 2018; 9:172.
12. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020. doi:10.1001/jama.2020.1585
13. Curbelo J, Luquero Bueno S, Galván-Román JM, et al. Inflammation biomarkers in blood as mortality predictors in community-acquired pneumonia admitted patients: importance of comparison with neutrophil count percentage or neutrophil-lymphocyte ratio. PLoS One 2017; 12:e0173947.
14. Liu X, Shen Y, Wang H, Ge Q, Fei A, Pan S. Prognostic significance of neutrophil-to-lymphocyte ratio in patients with sepsis: a prospective observational study. Mediators Inflamm 2016; 2016:8191254.
15. Berhane M, Melku M, Amsalu A, Enawgaw B, Getaneh Z, Asrie F. The role of neutrophil to lymphocyte count ratio in the differential diagnosis of pulmonary tuberculosis and bacterial community-acquired pneumonia: a cross-sectional

study at Ayder and Mekelle Hospitals, Ethiopia. Clin Lab 2019; 65.

16. Min CK, Cheon S, Ha NY, et al. Comparative and kinetic analysis of viral shedding and immunological responses in MERS patients representing a broad spectrum of disease severity. Sci Rep 2016; 6:25359.
17. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Semin Immunopathol 2017; 39:529–39.
18. Shaw AC, Goldstein DR, Montgomery RR. Age-dependent dysregulation of innate immunity. Nat Rev Immunol 2013; 13:875–87.
19. Moro-García MA, Alonso-Arias R, López-Larrea C. When aging reaches CD4+ T-cells: phenotypic and functional changes. Front Immunol 2013; 4:107.
20. Sakaguchi S, Miyara M, Costantino CM, Hafler DA. FOXP3+ regulatory T cells in the human immune system. Nat Rev Immunol 2010; 10:490–500.
21. Sakaguchi S. Regulatory T cells: key controllers of immunologic self-tolerance. Cell 2000; 101:455–8.