ORIGINAL ARTICLE

Comparison of Some Immunological Parameters of Covid-19 Patients with and without Diabetes According to age Groups and Gender

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ABSTRACT

During the Covid-19 epidemic, many variables affected the severity of infection, including age, gender, and chronic conditions. In this study, we compared the levels of some immunological parameters (IL6, IFNγ) in Covid 19 patients and diabetic patients with Covid 19 across age groups and gender.

Where the levels of interleukin-6 are higher than the normal range when infected with COVID-19 in all age groups and increased in patients without diabetes, where their levels are (210.04 ± 135.44). An increase in the level of IL6 indicates a severe infection with the COVID-19 virus, and this indicates transmission from moderate to severe or severe, as the results of the study did not show any significant differences at P>0.5, and IL6 levels increase in females than in males. Where it reaches (146.105±149.75)

The high rate of IFNγ production also indicates support for immunity against infection with the Covid-19 virus, and the equation of its production indicates a low survival rate for patients, as it is produced by helper T cells. JPY 0.009

Where the levels of IFNγ increase significantly in middle ages, reaching (157.64 ± 158.54), and the levels of IFNγ are close between females and males, as they are (102.7 ± 130.27) (102.2 ± 93.12), respectively.

Keywords: COVID-19 Patients; Interleukin-6; interferon gamma; diabetic patients.

INTRODUCTION

On December 31, 2019, the Chinese Health Authority alerted the World Health Organization to several cases of pneumonia of unknown cause in Wuhan City, Hubei Province, central China. On December 8, 2019, the cases were reported, and some patients worked or lived near the local Huanan Seafood Wholesale Market; However, other early cases are unrelated to this market (1).On January 7, a new coronavirus was detected from a patient's throat swab and initially designated as 2019-nCoV by the World Health Organization (2).This pathogen has been classified by the MERS-CoV Study Group (3).According to China's National Health Commission, the death rate among confirmed cases in China was 2.1 percent (4).Outside of China, the death rate was 0.2 percent (5).COVID-19 is a moderately contagious virus with a high mortality rate, despite the fact that the amount of information available in public reports and published studies is expanding all the time (6).Most patients who experienced severe cases of COVID-19 were obese, elderly people, or have chronic diseases such as pressure, diabetes, chronic lung and kidney lesions , Failure, heart lesions, immunodeficiency, or cancers.(7). Most studies have been conducted on COVID-19 patients refer to patients with diabetes and blood pressure Sick people are among the most vulnerable to infection with the virus. danger from Complications of diabetics, which lead to death, are very similar to having it ,Other types of SARS coronavirus and MERS-CoV , The incidence of type 2 diabetes in people with COVID-19 varies according to the average age and severity of infection illness.(8)

METHODS AND MATERIALS

Position of Study: Najaf Hospitals
The Studied Sample: Those infected with the Corona virus (Covid-19) in the city of Najaf.
Sample size: 64 patients coming to Najaf hospitals and 26 control.
Study Steps: Clinical examination and laboratory diagnosis.
Inclusion Criteria: People infected with COVID-19.
Exclusion Criteria: Persons with other secondary infection .
Sample collection: A sample of venous blood is collected in a test tube to measure D_dimer levels. Serum was isolated after centrifugation at 3500 rpm for 10 min.
IGG and IGM Test: serum of patient to diagnosis virus using SARS-CoV-2(COVID19)IgM & IgG VIDAS Kit from BioMérieux , France.
IFNΓ Test :- serum of patient to diagnosis virus using IFN- γ ELISA Kit BT LAB , China
IL6 Test:- serum of patient to diagnosis virus using IL6 ELISA Kit BT LAB , China

Statistical analysis: Data with SPSS instructions were processed, version 28 was considered statistically significant when the P-value was less than 0.05, and it was considered highly statistically significant when the P-value was greater than 0.01 (Cheskin, 2003) .

RESULT

The results showed that was non statistically significant (P>0.5) for an increase production of IL6 according to the age groups, as the highest rate of production of IL6 was in age group (C) and the lowest rate of production of IL6 was in age group (D), where the rate of production was (210.04 ± 135.44, 102.19±40.55), respectively.

The results also showed that the level rate of IL6 was increased in Covid-19 patients compared to diabetic patients with Covid 19 infection, as the highest production rate of IL6 in diabetic patients with Covid 19 infection was in the age group (B) and decrease the rate of IL6 had the age group (C) (175.33 ± 24.51, 91.30 ± 42.67), respectively.

Age groups	Concentration Of IL6 covid&diabetes mean±sd pg\ml	Concentration Of IL6 covid mean±sd pg\ml	Concentration Of IL6 postive control mean±sd pg\ml	Concentration Of IL6 negative control mean±sd pg\ml .
(A)	2(106.21±8.96)	2(151.73±10.10)	2(91.27±44.85)	2(133.69±7.37)
(B)	2(175.33±24.51)	4(158.38±181.32)	2(116.9 ± 56.8)	3(116.9 ± 56.8)
(C)	15(91.30±42.67)	4(210.04±135.44)	4(158.7 ±17.25)	3(137.6± 21.7)
(D)	13(125.64±89.57)	10(102.19±40.55)	4(145.85 14.5)	2(137.14±32.36)
(E)	9(132.80±123.25)	3(139.29±54.43)	2(139.01±11.16)	2(109.18±100.46)
Total	41	23	14	12

P< 0.5

A: age group 20= \ B: age group(21_35) \C: age group(36_50)\D: age group(51_65)\E: age group(66_80).

Table (1_1) shown IL6 of covid 19 patient in all groups

According gender the results showed insignificant differences in the levels of IL6 between the pathological groups, as the value of the P< 0.1, as the level of IL6 increased in females more than in males infected with Covid 19 infection, where the

average was (146.105 ± 149.75, 137.99 ± 84.98), respectively. Comparison with the control groups ,as well as results showed an increase in the levels of IL6 in diabetic patients with Covid-19 infection, males more than in females,

where levels were recorded (118.12 ± 91.73, 105.013 ± 73.85), respectively, compared with the control groups.

gender	Concentration Of IL6 covid&diabetes mean±sd pg\ml	Concentration Of IL6 covid mean±sd pg\ml	Concentration Of IL6 postive control mean±sd pg\ml	Concentration Of IL6 negative control mean±sd pg\ml
female	14(105.013±73.85)	7(146.105±149.75)	8(144.4105±22.98)	6(128.5±35.32)
male	27(118.12±91.73)	16(137.99 ± 84.98)	7(124.76±49.761)	6(108.13±36.48)
Total	41	23	14	12

P< 0.1

Table (1_2) shown IL6 of covid 19 patient in gender groups.

while the results showed insignificant differences of P< 0.01 in the level of IFNγ between the disease groups, where the levels of IFNγ were equal between males and females infected with Covid 19 infection, as the level of IFNγ in males and females was (102.2 ± 93.12, 102.7 ± 130.27), respectively.

As for diabetic patients with Covid-19 infection, the level of IFNγ increases in males than in females (76.9 ± 65.7, 75.57 ± 65.6), respectively.

gender	Concentration Of IFNγ covid&diabetes mean±sd pg\ml	Concentration Of IFNγ covid mean±sd pg\ml	Concentration Of IFNγ postive control mean±sd pg\ml	Concentration Of IFNγ negative control mean±sd pg\ml
female	14(75.57 ±65.6)	7(102.7±130.27)	8(66.23 ±17.7)	6(56.6±15.44)
male	27(76.9 ±65.7)	16(102,2±93.12)	7(49.15 ±9.8)	6(58.6±21.5)
Total	41	23	14	12

P< 0.01

Table (1_3) shown IFNã of covid 19 patient in gender groups.

Age groups	Concentration Of IFNã covid&diabetes mean±sd pg\ml	Concentration Of IFNã covid mean±sd pg\ml	Concentration Of IFNã postive control mean±sd pg\ml	Concentration Of IFNã negative control mean±sd pg\ml
A	2(28.71±8.56)	2(64.59±13.91)	2(48.27±2.75)	2(21.83±9.94)
B	2(58.39±4.32)	4(115.78±156.49)	2(68.67±2.65)	3(69.31±19.26)
C	15(58.70±17.68)	4(157.64±158.54)	4(65.75±17.97)	3(49.79±4.83)
D	13(96.70±64.86)	10(76.23±57.98)	4(54.43±18.05)	2(27.73±2.91)
E	9(91.05±105.51)	3(102.69±61.51)	2(74.10±21.82)	2(68.08±4.97)
Total	41	23	14	12

P< 0.009

Table (1_4) shown IFNã of covid 19 patient in all groups.

A: age group 20= \ B: age group(21_35) \C: age group(36_50)\D: age group(51_65)\E: age

The results showed high significant differences in the increase in the production of IFNγ at the P≤ 0.009 according to the age groups, as the level of IFNγ increases in age group (C) compared with other age groups, and the level of IFNγ decreases in age group (A) as the production rate is equal to (157.64 ± 158.54) (64.59 ± 13.91), respectively.

The results also showed significant differences in the increase in the level of IFNγ in patients with Covid 19 compared to diabetic patients with Covid 19 infection and control groups.

Whereas, the level of interferon increased in diabetic patients with Covid-19 infection in age group (D), and the level of interferon decreased in age group (A) (96.70 ± 64.86) (28.71 ± 8.56), respectively.

DISCUSSION

The emerging COVID-19 virus (SARS COV 2) is believed to most affect people with chronic diseases, including diabetics. This study amid the measurement of some parameters of immunity in patients with COVID-19 and the comparison of results with those with Covid19 patients with diabetes. This is according to age groups and gender.The study showed that the production rate of IL6 among Covid patients was higher compared to the control groups, as the production rate was (210.04 ± 135.44) in the age group (36-50), and there were no significant differences between the age groups P<0.5, and the rate of IL6 production was It is increased in non-diabetic covid patients than in diabetic patients with covid infection.As a omnidirectional cytokine, IL-6 enhances B-lymphocyte proliferation and differentiation while also increasing platelet synthesis. It also enhances the release of inflammatory substances such as C-reactive protein (CRP) and fibrinogen. IL-6 regulates the immune system, hematopoiesis, and inflammation, a key role in the cytokine storm that leads to death(9).The inflammatory response is critical in COVID-19 infection, and a storm of inflammatory cytokines exacerbates the disease. It has been argued that a cellular storm is necessary for the development of COVID-19 and can lead to significant problems and deaths (10).An increase in the level of IL6 indicates an acute infection of COVID-19, and this indicates transmission of infection from moderate to severe, and this is consistent with the study conducted by(11).One study(12) also showed that an increase in the rate of interleukin-6 production is accompanied by an increase in C-reactive protein levels, and this was proven by the results of our research. Although the pathophysiology of human coronaviruses (H-CoVs) such as SARS-CoV, MERS and SARS-CoV-2 is unknown, they have all been associated with a disturbed and excessive immune response, that is, cytokine production(13). It can be indicated that immune dysregulation is a very important point and therapeutic target for COVID-19 patients. The reasons for the large size of inflammatory cytokines are unclear, but they can play an important role in organ damage-associated apoptosis.

As well as that significant differences in the levels of IFNγ P≤ 0.009, where it is higher in Covid 19 patients in the age group (36-50) and by (157.64 ± 158.54) compared to Covid patients with diabetes, as well as higher than the control group.

The high rate of production of IFNγ indicates immunity support against infection with the Covid-19 virus, and the equation of its production indicates a low survival rate for patients, as it is produced by T-helper cells.(14). The cell's secretion of interferon-gamma helps stimulate the increased production of ACE2, which acts as a key to the entry of the virus into cells, and this leads to helping the virus to multiply indefinitely and makes the cell less resistant to the virus. (15). IFNγ is produced when sensitized cells are stimulated with an antigen or non-sensitized lymphocytes are stimulated with methogens , IFNγ possesses antiviral effect in addition to biological activities such as cell growth inhibition, immunosuppressive effects, increase of macrophages, natural killer (NK) cell, killer (K) cell, neutrophil functions, and differentiation-stimulating activity (16). This study is consistent with(17). The reason for the rise in IFNγ may be attributed to the end of the infection period, as it is considered an anti-inflammatory that increases in the last stages of infection.

CONCLUSION

There are no significant differences in the rate of interleukin-6 between age groups, as it is higher in females than in males, and interferon rates are higher in Covid patients of middle ages. They are close between males and females.

REFERENCES

1   Lu, H.,Stratton, C. W., and Tang, Y. W. (2020). Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. Journal of medical virology, 92(4), 401.

2   Hui, D. S., Azhar, E. I., Madani, T. A., Ntoumi, F., Kock, R., Dar, O., ... & Petersen, E. (2020). The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—The latest 2019 novel coronavirus outbreak in Wuhan, China. International journal of infectious diseases, 91, 264-266.

3   Brierley, L. (2020). The role of research preprints in the academic response to the COVID-19 epidemic. The role of research preprints in the academic response to the COVID-19 epidemic.

4   Harapan, H., Itoh, N., Yufika, A., Winardi, W., Keam, S., Te, H., ... and Mudatsir, M. (2020). Coronavirus disease 2019 (COVID-19): A literature review. Journal of infection and public health, 13(5), 667-673.

5   Jebril, N. (2020). World Health Organization declared a pandemic public health menace: a systematic review of the coronavirus disease 2019 "COVID-19". Available at SSRN 3566298.

6   Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... and Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet, 395(10223), 497-506.

7   Gao, Y. D., Ding, M., Dong, X., Zhang, J. J., Kursat Azkur, A., Azkur, D., ... & Akdis, C. A. (2021). Risk factors for severe and critically ill COVID-19 patients: a review. Allergy, 76(2), 428-455.

8   Singh, Awadhesh K., (2020): "Prevalence of co-morbidities and their association with mortality in patients with COVID-19: a systematic review and meta-analysis." Diabetes, Obesity and Metabolism 22.10:1915-1924

9   Tanaka T., Narazaki M., Kishimoto T;(2014): IL-6 in inflammation, immunity, and disease. Cold Spring Harb Perspect Biol. ;6:a016295.

10 Soy M., Keser G., Atagündüz P., Tabak F., Atagündüz I., Kayhan S;(2020): Cytokine storm in COVID-19: pathogenesis and overview of anti-inflammatory agents used in treatment. Clin. Rheumatol.:1–10. doi: 10.1007/s10067-020-05190-5.

11 Chen, X., Zhao, B., Qu, Y., Chen, Y., Xiong, J., Feng, Y., ... & Li, F. (2020). Detectable serum SARS-CoV-2 viral load (RNAaemia) is closely correlated with drastically elevated interleukin 6 (IL-6) level in critically ill COVID-19 patients. Clinical infectious diseases.

12 Liu F,.Li L, Xu M (2020). Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. **J. Clin. Virol.** 127, 104370.

13 Saadi, F., Pal, D., and Sarma, J. D. (2021). Spike Glycoprotein Is Central to Coronavirus Pathogenesis-Parallel Between m-CoV and SARS-CoV-2. Annals of Neurosciences, 09727531211023755.

14 Zhao J. Airway memory CD4(+) T cells mediate protective immunity against emerging respiratory coronaviruses. Immunity. 2016;44(6):1379–1391. doi: 10.1016/j.immuni.2016.05.006.

15 Shirley, R. (2008). Development of targeted gene delivery vectors to assess cardiac overexpresion of ACE2 in vivo (Doctoral dissertation, University of Glasgow).

16 Yamaji K, Nabeshima S, Murata M, Chong Y, Furusyo N, Ikematsu H, Hayashi J. Yamaji K, et al. Cancer Immunol Immunother. 2006 Apr;55(4):394-403. doi: 10.1007/s00262-005-0005-x. Epub 2005 Jul 22. Cancer Immunol Immunother. 2006. PMID: 16041541 Clinical Trial.

17 Cardona, P. J., Caylà, J. A., Hernández, A., Palma, D., and Rius, C; 2021. Revisión sobre las vacunas frente a SARS-CoV-2. Actualización a 31 de enero de.