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The Potential Role of Interferon-Alpha in Severity of Coronavirus Disease 2019

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Abstract

The main point in COV-2 infection could be depletion of natural antiviral defenses, as well as the elevated cytokines secretion. IFN disruption is a crucial factor in COVID-19 pathology, according to recent research. The goal of this research was to elucidate interferon-alpha concentration, as well as to examine its association with COVID-19 severity. This case-control research included eighty-five subjects (fifty patients with SARS-CoV-2 and thirty-five controls) with age range (18-77) years old. The oral hygiene index was used to determine oral health. The levels of IFN- were measured in serum using an ELISA. This study showed decrease ($P<0.03$) in IFN-alpha among patients compared to controls. Also, a highly considerable difference ($p<0.001$) in IFN-alpha concentration among patients' groupings, with no significant difference between the moderate and mild groups. Furthermore, there was no significant variation in interferon-alpha levels between good oral hygiene and those with poor oral hygiene ($p=0.35$). A Significant decrease in interferon-alpha among patients provides evidence of inappropriate immune response in patients, and the association of low interferon-alpha with the severity of disease indicated that this cytokine can be utilized as biomarkers of disease activity.

The optical properties of CdS NPs such as the coefficient of absorption, refraction, and diffraction were calculated using mathematical equations.

Keywords: corona virus; innate immune response; cytokines; oral health; viral infection.

1. Introduction

The 2019 novel coronavirus (2019-nCoV), which causes acute respiratory disease (ARD), first surfaced in Wuhan in December and quickly spread across the rest of China [1]. The virus belongs to the genus Beta-coronavirus, which is part of the Coronaviridae family, which is part of the Nidovirales order. Infection with SARS-CoV-2 induces immune response malfunction in humans, such as the quick release of many cytokines into body fluids, resulting in ARDS and multiple organ

failure [2,3]. Clinical classifications for the SARS-CoV-2-caused COVID-19 include mild, moderate, severe, and critical [4,5].

COVID-19 infects thousands of people, which can have fatal consequences not only for those who are already ill, also for healthy young adults with a strong immune system. This particular coronavirus appears to have unique capacities to propagate and damage human immune systems [6-9]. The virus spreads and destroys infected tissues because lack of protective immune response, particularly in regions with high ACE2 expression. The innate inflammatory response that is brought on by damaged cells in the lungs is primarily mediated by granulocytes and pro-inflammatory macrophages. Lung inflammation is the root cause of life-threatening respiratory diseases at the advanced stage [10]. Determining Interferon levels and determining whether they were associated with the severity of COVID-19 was the goal of this study as a result.

2. Materials and Methods

2.1 Study Design: case control study

2.2 Study Population

Fifty COVID-19 patients, aged 18 to 77, participated in this study, with 29 men and 21 women. From November 2020 to January 2021, all cases were retrieved from Ibn AL-Khateeb hospital in Baghdad governorate. All of the patients had SARS-CoV-2 infection, in accordance with World Health Organization guidelines [11]. The SARS-CoV-2 infection was found using a RT-PCR. Patients were categorized into mild, moderate, and severe disease based on the clinical management criteria specified in the diagnosis and treatment protocol for COVID-19. Patients had to be infected with COVID-19 and have COVID-19 RT-PCR as well as exhibit COVID-19 infection symptoms (fever, widespread malaise, cough, and difficulty breathing) included in this study. Patients with chronic sinusitis, allergic rhinitis, and persistent viral infections as well as those who were unable to provide informed consent were excluded from this study. The controls group was made up of 35 people (16 men and 19 women); their ages and sexes were matched to those of the patients, whose ages ranged from (18 to 73 years).

2.3 Evaluation of Oral Hygiene

For the evaluation of dental hygiene, the simplified oral hygiene index was used."Oral Hygiene Index = Debris Index + Calculus Index" [12].

2.4 Collection of Specimens

Four milliliters of blood were drawn from each participant. The serum was separated from the blood by centrifuging it at 3000 rpm for 10 minutes, and it was then kept at -20 °C until analysis.

2.5 Detection of IFN-α

Serum IFN-α was measured by ELISA and carried out in accordance with the directions in the kit's instruction manual (Bioassy technology/China).

2.6 Statistical analysis

Histograms and the Smemirnove-Kolmogorove test showed that the data was non-parametric and described by the median; therefore, non-parametric tests of significance were advised. Using a 0.05 P value, the statistical significance was calculated.

3. Result

3.1 Serum level of IFN- α in patients and controls

The current study discovered that patients with COVID-19 had significantly lower median serum levels of IFN- α than healthy controls (P<0.05). The median level of IFN-α across patient subgroups also showed a highly statistically considerable variation (p<0.05); for severe cases, this level was (156 pg/ml), for moderate cases, it was (270 pg/ml), and for mild cases, it was (331 pg/ml), table (1).

Table 1: Difference in Levels of IFN-α in Studied Group.

Serum IFN-α	Study groups		Sig.
	Patients N=50	Controls N=35	
Minimum	104	118	0.037*
Maximum	566	648	
Median	264	304	
Mean Rank	38.34	49.66	

3.2 Serum Level of IFN- A in Patients According to Severity

As shown in table (2), there is no significant difference between the moderate and mild groups, but there is a substantial distinction (p<0.05) between the severe group and the moderate and mild groups.

Table2: levels of IFN-α in patients across disease severity

Serum IFN	Patients group			
	Severe n=10	moderate n=29	Mild n=11	Sig.
Min	108	111	104	0.001**
Max	262	511	566	
Median	156	270	331	
Mean Rank	13.95	22.09	13.23	
Severe X moderate				0.009**
Severe X mild				0.013*
Moderate X mild				0.133^{NS}

3.3 Serum level of IFN- α in patients according to oral health

Moreover, the result also showed the no a substantial disparity ($p>0.05$) in IFN-α levels among subjects with good oral health (269.5 pg/ml) and in subjects poor oral health (255.5 pg/ml), table (3).

Table 3: levels of IFN-α in patients with oral health.

Serum IFN-α	Good N=18	Poor N=32
Min	135	104
Max	410	566
Median	269.5	255.5
Mean Rank	28.08	24.05
P-value	0.352^{NS}	

4. Discussion

SARS-CoV-2 infection research is currently of the utmost importance to scientific organizations around the globe. In light of this, we made the decision to research IFN-'s function in COVID-19 patients at various disease stages. Although this was the main goal of our research, we also considered

how oral health status in COVID-19 patients compared to healthy controls. One relevant pathway implicated in severe COVID-19 symptoms is a lack of interferon responses. The current findings revealed that the blood IFN- level in people infected in this disease was much lower as compared to healthy people, and that the level declined as the severity of the disease increased. The low level of serum IFN- in this study could be attributable to SARS-antagonistic CoV-2's mechanisms, which are similar to those seen in other severe human COVs such as (severe acute respiratory syndrome and Middle East respiratory syndrome), which prevent the host from sending IFN signals particularly type I IFN production [13].

Along with persistent viremia and an exaggerated inflammatory response in response to elevated pro-inflammatory cytokines (TNF and IL-6), the impaired type I IFN response was also characterized by decreased IFN expression in both SARS-CoV-2-infected human bronchial cells and circulating mononuclear blood cells [14]. These findings support a previous study conducted by Hadjadj et al.

(2020), who found that serum IFN levels in COVID-19 patients were significantly lower than in non-COVID individuals, and that serum IFN activity was significantly lower in severely or critically ill patients than in mild to moderate patients [15]. Furthermore, a rise in serum IFN- levels in COVID-19 patients was linked to a reduction in disease severity and enhanced survival [16]. Other investigations 17,18]. showed that severe stage of disease had an extended IFN-alpha response and a stable inflammatory reaction in their blood. The heterogeneity of IFN- responses in patients could brought on by the disparity of illness severity standards and varied sampling times during disease development [19].

There were no differences in concentration of IFN in infected individuals with adequate and bad oral health, according to this research. People with bad oral health are more likely to develop periodontitis, as there is a strong link between bad oral health and the buildup of dental plaque, which is a risk factor for periodontitis [20]. Furthermore, Mizraji et al. shown that periopathogens cause periodontal disease by disrupting the equilibrium of the host-oral microbiota. It is believed that few concentrations of IFN-alpha generated shortly after infection are thought to be crucial for the development of cellular immune response in the case of bacterial infection [21, 22]. However, no previous research backs up this conclusion.

6. Conclusions

A Significant decrease in interferon-alpha among patients provides evidence of inappropriate immune response in patients, and the association of low interferon-alpha with the severity of disease indicated that this cytokine can be utilized as biomarkers of disease activity.

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References:

[1] Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-1720. doi: 10.1056/NEJMoa2002032.

[2] Sun H, Guo P, Zhang L, Wang F. Serum Interleukin-6 Concentrations and the Severity of COVID-19 Pneumonia: A Retrospective Study at a Single Center in Bengbu City, Anhui Province, China, in January and February 2020. Med Sci Monit. 2020 Nov 11;26:e926941. doi: 10.12659/MSM.926941.

[3] Tu YF, Chien CS, Yarmishyn AA, et al.. A Review of SARS-CoV-2 and the Ongoing Clinical Trials. Int J Mol Sci. 2020 Apr 10;21(7):2657. doi: 10.3390/ijms21072657.

[4] Li K, Fang Y, Li W, et al. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol. 2020 Aug;30(8):4407-4416. doi: 10.1007/s00330-020-06817-6.

[5] Yang X, Yu Y, Xu J, 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 May;8(5):475-481. doi: 10.1016/S2213-2600(20)30079-5.

[6] Savan R, Gale M Jr. Innate immunity and interferon in SARS-CoV-2 infection outcome. Immunity. 2023 Jul 11;56(7):1443-1450. doi: 10.1016/j.immuni.2023.06.018.

[7] Tanveer A, Akhtar B, Sharif A, Saleem U, Rasul A, Ahmad A, Jilani K. Pathogenic role of cytokines in COVID-19, its association with contributing co-morbidities and possible therapeutic regimens. Inflammopharmacology. 2022 Oct;30(5):1503-1516. doi: 10.1007/s10787-022-01040-9.

[8] Adham, ZS and Al-Ghurabi, BH. Prevalence of viral co-infection among COVID-19 cases in association disease severity and oral hygiene. J Bagh College Dentistry. 2021:33(3). https://doi.org/10.26477/jbcd.v33i3.2947.

[9] AL-Ghurabi BH, Adham ZS, Abbas AA. Level of b-defensin among Iraqi patients with COVID-19 in relation to oral health status, Journal of Emergency Medicine, Trauma & Acute Care. 2022;(2):2. doi: https://doi.org/10.5339/jemtac.2022.ismc.2

[10] AL-Ghurabi BH. The Role of Soluble TLR-2 in the Immunopathogenesis of Gingivitis. International Medical Journal. 2021; (1994): 28.

[11] Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, & Chen Q. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. International journal of oral science. 2020;12(1):1-5. doi: 10.1038/s41368-020-0074-x

[12] World Health Organization. Coronavirus disease 2019 (COVID-19). 2020

[13] Greene JG and Vermillion JR. The simplified oral hygiene index. The Journal of the American Dental Association. 1964;68(1):7-13. doi: 10.14219/jada.archive.

[14] Ribero M, Jouvenet N, Dreux M, & Nisole S. Interplay between SARS-CoV-2 and the type I interferon response. PLoS pathogens. 2020;16(7): e1008737. https://doi.org/10.1371/journal.ppat.1008737

[15] Wang Y, Wu M, Li Y, Yuen HH, He ML. The effects of SARS-CoV-2 infection on modulating innate immunity and strategies of combating inflammatory response for COVID-19 therapy. J Biomed Sci. 2022 May 3;29(1):27. doi: 10.1186/s12929-022-00811-4. PMID: 35505345; PMCID: PMC9063252.

[16] Hadjadj J, Yatim N, Barnabei L, et al. Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. Science. 2020 Aug 7;369(6504):718-724. doi: 10.1126/science.abc6027.

[17] Contoli M, Papi A, Tomassetti L, et al. Blood Interferon-α Levels and Severity, Outcomes, and Inflammatory Profiles in Hospitalized COVID-19 Patients. Front Immunol. 2021 Mar 9;12:648004. doi: 10.3389/fimmu.2021.

[18] Lee JS, Park S, Jeong HW, et al. Immunophenotyping of COVID-19 and influenza highlights the role of type I interferons in development of severe COVID-19. Sci Immunol. 2020 Jul 10;5(49):eabd1554. doi: 10.1126/sciimmunol.abd1554

[19] Lucas C, Wong P, Klein J, et al. Longitudinal analyses reveal immunological misfiring in severe COVID-19. Nature. 2020 Aug;584(7821):463-469. doi: 10.1038/s41586-020-2588-y.

[20] Lee JS, Shin EC. The type I interferon response in COVID-19: implications for treatment. Nat Rev Immunol. 2020 Oct;20(10):585-586. doi: 10.1038/s41577-020-00429-3.

[21] Qi X, Northridge ME, Hu M, Wu B. Oral health conditions and COVID-19: A systematic review and meta-analysis of the current evidence. Aging Health Res. 2022 Mar;2(1):100064. doi: 10.1016/j.ahr.2022.100064. Epub 2022 Mar 5. PMID: 35281130; PMCID: PMC8896863.

[22] Mizraji G, Nassar M, Segev H, et al. Porphyromonas gingivalis Promotes Unrestrained Type I Interferon Production by Dysregulating TAM Signaling via MYD88 Degradation. Cell Rep. 2017 Jan 10;18(2):419-431. doi: 10.1016/j.celrep.2016.12.047.

[23] Kareem HH, Al-Ghurabi BH, Albadri C. Molecular Detection of Porphyromonas gingivalis in COVID-19 Patients. J Bagh Coll Dent. 2022 Jun;34(2):52-61. https://doi.org/10.26477/jbcd.v34i2.3145.

[24] Al-Ghurabi BH, Mohssen SM: Salivary level of RANKL and OPG in chronic periodontitis . JBDC. 2015, 325:1- 12