HNSJ Humanities & Natural Sciences Journal
ISSN: (e) 2709-0833
www.hnjournal.net

Peer-Reviewed Journal
Indexed at: NSP - SJIF
Impact Factor 2022 = 4.91

RESEARCH TITLE

Linking Inflammatory Biomarkers to COVID-19 Outcomes: The Role of Procalcitonin, IL, IFN-γ, and CRP.

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HNSJ, 2024, 5(11); https://doi.org/10.53796/hnsj511/20

Published at 01/11/2024 **Accepted at 20/10/2024**

Abstract

Abstract: The expansion of COVID-19 depends seriously on inflammatory reactions, which are exacerbated by the inflammatory cytokine storm. This study aimed to assess the effect and concentrations of procalcitonin, IL-10, CRP, and IFN in individuals infected with COVID-19. Individuals recently diagnosed with COVID-19 exhibited an increased risk of disease progression, characterized by (P:<0.05), significantly elevated mean of procalcitonin levels in comparison with non-infected individuals (88.18+4.62 Vs.24.51±3.28pg/ml). The study established that a new diagnosed COVID 19 patients exhibited significantly higher levels of IL-10 compared to healthy controls (43.5±5.74 Vs. 27.6±4.23 pg/ml). Also, IFN-Gamma levels are much higher in newly infected COVID-19 patients in comparison with non-infected persons (38.32±5.43 v.s.22.41+4.31pg/ml) with P value < 0.05. A significant increase was found in CRP levels in patients with new COVID -19 infection compared to healthy controls (63.4 ± 8.22 vs. 8.17 ± 2.33 mg/dl) (P:<0.05). The investigators found a clear correlation between COVID 19 and procalcitonin, IL-10, IFN gamma, and CRP within the first week of contamination.

Key Words: *Biomarkers; procalcitonin; IL-10; IFN- γ;* COVID-19

1. Introduction

The World Health Organization declared that countries should prepare for a pandemic due to coronavirus disease in early 2020- COVID19 (new coronavirus infection). Since then numerous studies ranging from epidemiological to experimental works have been published an attempt for understanding the immune pathways and potential treatments for COVID-19. The number of CD3+, CD4+, and CD8+ lymphocytes decreases with disease stage [(1)]. Furthermore, critically ill patients experience cytokine storms as a result of increased levels of interleukins like TNF ,and interleukeins 6, 8, and 10 are all cytokines that promote inflammation [(2,3)] Changes in COVID19 severity are connected to differences in the immunological response of the host. Severe COVID-19 infection has been linked to increased C-reactive protein, albumin, blood urea nitrogen lactate dehydrogenase and bilirubin levels that considered as a predictive agents [(4)]. Interleukins are classified as prognostic variables, where IL-6, IL-8, and IL10 identified as predictive pointers in COVID-19 affected persons, it's plausible to assume that I proinflammatory innate immunity and (ii) anti-inflammatory immunity were linked to death and severity of the illness [(1,3,5)]. Although cells are in distinct phases of the immune reaction, IFN type II that formed by NK cells and T-lymphocytes, and it is significant in all steps of the immune reaction. Antiviral resistance relies heavily on the IFN-system. IFN- inhibits viral replication and stimulates T cells to release cytokines, allowing them to kill cytotoxic T cells more effectively. A rise concentration of IFN aggravate a systemic inflammation, leading to increased tissue injury and organ impairment [(6)]. A single-center study showed an increase in many markers of inflammation in patients with intensive care units [(7)] or people with significant disease ([8,9,10]) vs. those with less serious disease. White blood cell count, procalcitonin (PCT) levels, C-reactive protein (CRP), interleukin 6 (IL-6) and interleukin 10 levels are among the signs (IL-10). Patients with elevated PCT were also nearly 5 times as probable to get severe symptoms, according to the meta-analysis. [(11)] so the purpose of this current work is to assess procalcitonin, IL-10, IFNγ and CRP levels in COVID19 infected individuals.

2. Materials and Methods

Forty patients aged 20-80 years and 40 healthy patients in the similar age group were enrolled in this study, using ELISA technology (Koma biotech, ELISA, USA) for the detection of procalcitonin, IL-10, IFN -γ and CRP, correspondingly). Get all the necessary information from patients and healthy people; as sex, old, life situation, family members in addition to medical history, and journeys to infected areas by taking 5 ml of venous blood from them. The immune responses of the two groups were compared using the features listed above.

3. Results and Discussion

This research involved 40 person established with COVID -19 (+ ve) and 40 healthy person (COVID -19 free), there was an important difference between infected persons and the healthy persons concerning Procalcitonin level with P value < 0.05 as in table.(1).

Table 1- Procalcitonin level in COVID19 patients and healthy peoples

Group	Mean [pg/ml]	SD	P-Value
COVID 19 Patients	88.18	4.62	< 0.05
Healthy peoples	24.51	3.28	

In addition, the study showed that individuals with COVID-19 had significantly higher IL-10 concentrations than healthy controls [43.5±5.74 Vs. 27.6±4.23 pg/ml (P<0.05), Table 2.

Table 2- concentrations of IL-10 in COVID19 subjects and healthy people

Groups	Mean[pg/ml]	SD	P-Value
COVID 19 Patients	43.5	5.74	< 0.05
Healthy peoples	27.6	4.23	

The work established that IFN-Gamma concentrations was higher in individuals with COVID -19 in comparison with healthy individuals (38.32±5.43 v.s.22.41±4.31pg/ml) (P <0.05), Table 3.

Table3- IFN-Gamma in patients with COVID-19 and Healthy peoples

Groups	Mean[pg/ml]	SD	P-Value
COVID 19 Patients	38.32	5.43	< 0.05
Healthy peoples	22.41	4.31	

This work revealed that CRP levels were massively risen in COVID19 infested people compared with healthy controls (63.4 ± 8.22 vs. 8.17 ± 2.33 mg/dl) (p<0.05), Table 4

Table 4: Mean of CRP in COVID - 19 patients and Healthy peoples

Groups	Mean[pg/ml]	SD	P-Value
COVID 19 Patients	63.4	8.22	< 0.05
Healthy peoples	8.17	2.33	

Table: 5- C-reactive protein correlation with every work parameter

Parameter	R value
Procalcitonin	*0.83*
IL-10	*0.63*
IFN -Gamma	*0.55*

Discussion:

In COVID19, the inflammatory process is crucial, and an inflammatory cytokine wave exacerbates the condition (12,13). Wan and his colleagues (14) discovered that cytokine storm is essential for COVID19 development, and that it can lead to significant illness and death. CRP is a biomarker for inflammatory process, illness, and tissue destruction that is highly sensitive. It's a generic acute cycle protein that IL-6 causes in the liver. CRP levels are normally low, but during chronic inflammatory reactions, they spike dramatically and considerably. (15). CRP raise alone or conjoining with additional indicators, may possibly advocate viral or bacterial illness. This research looked into the connection among CRP and COVID19, discovered that peoples with a CRP of 63.4 mg/dl were had a higher chance to develop severe disease than those with an 8.17 mg/dl CRP (p-value 0.05). According to PCT, the patient group had a higher level of 88.18 pg/ml than the healthy group, 24.51 pg/ml and p. Values < 0.05. Procalcitonin (PCT) is a glycoprotein with no hormonal action and calcitonin precursor. Concentrations of serum PCT are frequently low or unnoticeable. Bacterial infections increase PCT levels (15). Many investigations have discovered that highly concentrations of PCT is connected to the severity of COVID-19 (16,2). Greater PCT concentrations were similarly linked to a 5-fold increased hazard of COVID-19 severity, according to the meta-analysis (11). According to IL-10 the level in the patients were 43.5 pg /ml high than that in healthy peoples 27.6 pg /ml with p. value <0.05. IL-10, High levels of IL-10, cease activity and development of immune cells and delaying viral clearance (17). As a result, high levels of IL-10 could be to blame for normal levels of IFN-g, a virus-clearing cytokine. IL-10 inhibitors should also be considered in the treatment of COVID-19. Other research suggests that excessive amounts of those cytokines and additional inflammatory factors can progress to produce so-called a cytokine storm(18, 19). Viral multiplications in upper respiratory tract cells until reaches the inner pulmonary tissue, this increased secretion of cytokines can lead to bulimia leading to SARS-CoV-2 associated respiratory distress syndrome. After a virus that induces traditional immunity to viruses and a linked with a probable peak of T-cell response, nevertheless, it is unclear whether immune overactivity or fail to respond to inflammatory reaction because of persistent immune dysregulation or viral replication is at the root of disease severity(20). To determine the role of immunity to Covid-19 many up-to-date responses suggest that IL-6 and C-reactive protein are higher in COVID-19 patients, especially individuals with diabetes and comorbidities as vascular pain and chest pain (21,22). Additional studies have found that two conditions caused by viral infection and proliferation of respiratory epithelial cell are high levels of virus-related acid inflammation and vascular leakage, as proved in SARS-CoV patients. Prostatitis; is a sever inflammatory form of programmed cells death, regularly seen through cytokine containing viruses that is a possible induction for a future inflammatory reaction (23). It is claiming to notice that a further study directed in It's worth mentioning that a new report showed that people with acute Covid19 had the peak serum levels of inflammatory cytokines, CRP and IL-6when compared with people with minor cases, analogous to the results confirmed in our work, that found a high positive (24). Some researchers think that the development of these infections, along with other unknown mechanisms, could have played a crucial role in autoimmune fluctuations and then main resistance in patients infected with the new Covid19. Modification in laboratory markers, for example higher blood values of cytokines and chemokines, as well as elevated CRP in the infected patients were related to severity of the illness and its consequences (24).

Conclusions

This study highlights the significant role of inflammatory biomarkers-procalcitonin, IL-10, IFN-γ, and CRP- in assessing the severity and progression of COVID-19. The noticeable elevation of these markers in newly diagnosed patients underscores their potential as prognostic indicators. Specifically, the observed increase in procalcitonin and cytokines such as IL-10 and IFN-γ advocate a heightened inflammatory response, which is characteristic of the cytokine storm associated with severe COVID-19 cases. Moreover, elevated CRP levels further correlate with disease severity, reinforcing the importance of monitoring these biomarkers in clinical settings. Our results support the inclusion of these inflammatory markers in standard evaluations of COVID-19 patients in order to enhance risk assessment and guide treatment plans. All things considered, early detection of increased inflammatory markers may offer vital information about the course of the illness and direct clinical judgment when treating COVID-19.

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