Journal of Applied and Natural Science
15(2), 538 - 541 (2023)
ISSN : 0974-9411 (Print), 2231-5209 (Online)
journals.ansfoundation.org

Research Article

Human leukocyte antigen-C (HLA-C) serum level as an indicator of severity among acute respiratory syndrome coronavirus patients

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Article Info
https://doi.org/10.31018/jans.v15i2.4398
Received: January 14, 2023
Revised: April 29, 2023
Accepted: May 5, 2023

How to Cite

Habeeb, R. F. and Al-Khafaji, N. S. K. (2023). Human leukocyte antigen-C (HLA-C) serum level as an indicator of severity among acute respiratory syndrome coronavirus patients. *Journal of Applied and Natural Science*, 15(2), 538 - 541. https://doi.org/10.31018/jans.v15i2.4398

Abstract

One of the respiratory viruses with the highest rate of dissemination, the coronavirus, sparked a global pandemic that claimed the lives of roughly six million people. As a result, various vaccinations and medications to lessen disease severity and hasten patient recovery were developed quickly. The purpose of this study was for coronavirus patients with acute lung distress to have their serum levels measured and compared to healthy controls. One hundred eighty blood samples from respiratory infections syndrome coronavirus patients between the ages of (13-80) were included in this case-control research. Results showed that human leukocyte antigen-C (HLA-C) serum concentrations were measured in patient groups compared to healthy groups. Patients with acute lung symptoms of coronavirus had higher serum levels of HLA-C, and the outcomes were contrasted using the Kruskal-Wallis. Upon testing, it was discovered that their serum levels for HLA-C showed a significant difference (P< 0.05). There were severe corona patients without pneumonia having a level of 40.03 ng/ml, severe corona patients with pneumonia having a level of 47.93ng/ml, non-severe corona patients without pneumonia having a level of 46.83 ng/ml, non-severe corona patients with pneumonia cases having a level of 61.15 ng/ml and with controls having a level of 17.65 ng/ml, (P ≤0.001). An increase in HLA-C serum level led to contribute to the immune storm that changes immunoregulatory such as including reducing the number of allogeneic made by mixing lymphocyte cultures, death of the natural killer cell and CD8+ T lymphocytes, and inhibition of alloreactive cytotoxic T lymphocytes (CTL) activity.

Keywords: Acute respiratory syndrome coronavirus, ELSA test, Human leukocyte antigen (HLA-C), Pneumonia

INTRODUCTION

The novel severe acute pulmonary symptoms of coronavirus, SARS CoV-2 are what causes COVID-19, which has significant rates of morbidity and fatality (Wang *et al.*,2021). One of the most important immune responses is innate and adaptive crucial and essential hosting variables for preventing COVID-19 and SARS-CoV-2 infections) Hosseini *et al*., 2020). Studies have shown that people with COVID-19 exhibit dysregulated immune responses that manifest as a potentially fatal systemic inflammatory syndrome (SIS) and hyper-inflammatory immunological humoral reactions characterized by cytokine storms (Costela-Ruiz *et al*., 2020; Tahaghoghi-Hajghorbani *et al*., 2020). In addition, there are compromised cellular antiviral immune responses! (Zhang *et al*., 2021). The molecular pathways behind the downregulation of individuals with COVID-19 have immunological reactions that are poorly understood. Severe acute respiratory might have developed many strategies to evade host antiviral immunity during viral infection, hence promoting virus reproduction and disease development (Lin *et al*., 2021), both innate and, adaptive immune cells that are usually active emerge during a viral infection. Among the reactive innate immune cells, natural killer (NK) cells are engaged in destroying infections,!virus infected cells, and the inhibition of viral transmission. Following activating CD8+ cytotoxic T lymph cells with virus-specificity, virus-infected cells are specifically killed and virus-specific CD4+ T lymphocytes are also triggered. Human leukocyte antigens (HLA) are a crucial controller of naturally occurring killer cells and T - cell stimulation (De Wit *et al*., 2016). HLA are two types of highly polymorphic cell surface molecules: I and II! (Trowsdale and Knight, 2013). The two subtypes

of HLA-classI molecules-classic (HLA-A, B, and C) and non-classic can be roughly classified (HLA-F, G, H, and E_included)) Abualrous *et al*.,2021)."Conventional HLA class I represents the strongest components of when immune system's defense prevention of viral infections. They participate in the activation,!differentiation, as well as amplification of T lymphocytes by exposing them to viral epitopes and promoting their growth into potent antiviral cells(Imrie and McCarthy, 2021). Contrarily, non-classical HLA-class I molecules seem to serve immunosuppression purposes primarily (Wyatt *et al*., 2019).

The immune system's correct operation depends on the human leukocyte antigen complex (HLA), which comprises a group of extremely variable genetic variants that have been linked to a broad range of illnesses. HLA class, I molecules deliver intracellular peptides originating from hosts and pathogens to immune system effector cells, causing immunological compassion under wholesome circumstances but rather generating efficient abnormal immunological activation. Only found in both people and big apes. The HLA-C is the most recently developed*HLA class I gene (Meuleman *et al.,* 2018). HLA-C differs compared to its family members, HLA-A and HLA-B, in that it shows unique characteristics in its expression and interaction with other molecules. There are numerous killer cell immunoglobulin-like receptors (KIRs), and NK cells are the main cells that produce them and recognize HLA-C as a natural ligand A growing body of research shows that NK cells are essential for the initial management of viral infections but also that connections among HLA-C and thus its corresponding KIR ligands impact the outcome of a course of viral infections (Vollmers *et al*.,2021). HLA-C heterodimers consist of two polypeptide chains, α, likewise β2-microglobulin. The membrane serves as the anchor for the hefty link, by displaying peptide first from the endoplasmic reticulum lumens HLA ClassI elements play a crucial function in the immune systems. HLA C genes serve to display intracellular proteins to cytotoxic T cells (CTLs) (Hansen and Bouvier, 2009). Numerous research studies have shown increased HLA gene concentration in various pathology, especially autoimmunity, cancerous, and infectious disorders, and their correlation with symptom severity or results (Kubysheva *et al*., 2018). The present study aimed to determine the Human leukocyte antigen-C (HLA-C) serum level to indicate severity among acute respiratory syndrome coronavirus patients.

MATERIALS AND METHODS

Sample collection

One hundred and eighty blood specimens from acute respiratory syndrome coronavirus patients and healthy groups with ages between (13-81) years were divided into groups based on how severe each condition was: 40severe corona patients without pneumonia,40 severe corona patients with pneumonia, 40 non-severe corona patients without pneumonia, 40 non-severe corona patients with pneumonia and 20 controls. All groups of COVID-19 patients had positive results for PCR tests and positive results for *Streptococcus pneumoniae* and *Klebsiella pneumoniae* in patients with bacterial infections who had spent two months receiving care during COVID-19 Units at Merjan Health City, and Emam Sadeq Hospital in Babylon Province (December 2021 and January 2022). Five ml of venous blood from each individual was extracted, sterilized ethanol at 70% was applied to the skin above the vein, and then put into a Gel tube to separate the blood. The blood underwent a five-minute, 3000 rpm centrifugation after 30 minutes at room temperature. After that, the sera were split into two relays and put in clean Eppendorf tubes. It was then stored there while being refrigerated below -20 °C.

Immunological analysis

The company's recommendations state an ELISA kit was used to determine the levels of HLA-C in serum in vitro (Korean Biotech CO.). 0.2 ng/ml was the lower limit of detection.

Ethical consideration

After receiving with necessary consent from government officials, the approvals were taken from all participants. The following facts were noted: Profile, Age, Gender, Infectious period, as well as Chronic illness.

Statistic evaluation

Graph Pad Prism edition 9.5.0 and IBM SPSS Statistics 26.0 (Armonk, NY: IBM Corp.) were used for the statistics (San Diego, California USA). The significance of variations among medians was determined using the Mann-Whitney-U test (to compare two groups) or the Kruskal-Wallis test (to compare more than two groups). Statistical significance was defined as a probability (P) value of 0.05.

RESULTS AND DISCUSSION

HLA-C serum level calculation in COVID-19 cases

Patients with COVID-19 can be cured by mounting a powerful protective immunity that can contain the infection and by receiving the right care. The current findings showed that there was a large difference ($P \leq 0.05$) in the serum levels of HLA-C between patients and healthy controls. The present research showed that serum HLA-C levels were noticeably increased among acute respiratory syndrome coronavirus patients regardless of disease severity. TheiHLA-C serum levels were significantly increased in acute respiratory syn-

drome coronavirus, severe corona patients without pneumonia having a level of 40.03 ng/ml, severe corona patients with pneumonia having a level of 47.93 ng/ml, non-severe corona patients without pneumonia having a level of 46.83 ng/ml and non-severe corona patients with pneumonia having a level of 61.15 ng/ml compared to the controls 17.65 ng/ml, (P≤ 0.001), as shown in Table 1. In the case of disease severity, Patients with severe without pneumonia, severe with pneumonia, non-severe without pneumonia, and non-severe with pneumonia have significantly different HLA-C values (p ≤ 0.000) (Fig. 1).

These results were mostly in line with the earlier discovery that patients suffering from severe illness had upregulated HLA-C blood levels (Al-Bayatee, and Ad'hiah,2021). These findings support recently discussed creative theories linking HLA-C to COVID-19 immunopathogenesis and symptom severity (Saulle *et al*., 2021). HLA-C can act as both an activator and a blocker of T regulatory cells and NK cell cytotoxicity under physiologically normal circumstances (Bian and Fu, 2022). A human pulmonary epithelial carcinoma cell that was SARS-CoV-infected was discovered to have a surprising number of genes associated with HLA-classI (including HLA-C) HLA classII or increased antigen expression 36 hours after infectious (Josset *et al*., 2013).

Nelde *et al*. (2022) confirm the present study's findings and indicate more research into serum HLA class I levels and their relationship to various symptoms. Elevated serum HLA class I levels were significantly associated with COVID-19 symptoms, such as cough, headache, and fatigue, reported by convalescent individuals.

Conclusion

The present study concluded that HLA-C is involved in the pathogenesis of acute respiratory syndrome coronavirus infection. It is one of the factors that can cause individuals with respiratory distress caused by the coronavirus to acquire severe and deadly illnesses.

Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1. Estimation of HLA-C serum levels among acute respiratory syndrome coronavirus patients

Type of patients	No. of patients	HLA-C ng/ml (Mean Rank)	P-value
Severe	40	40.03	
Sever Pneumoniae	40	47.93	
Non-severe	40	46.83	0.001
Non-severe Pneumoniae	40	61.15	
Control	20	17.65	

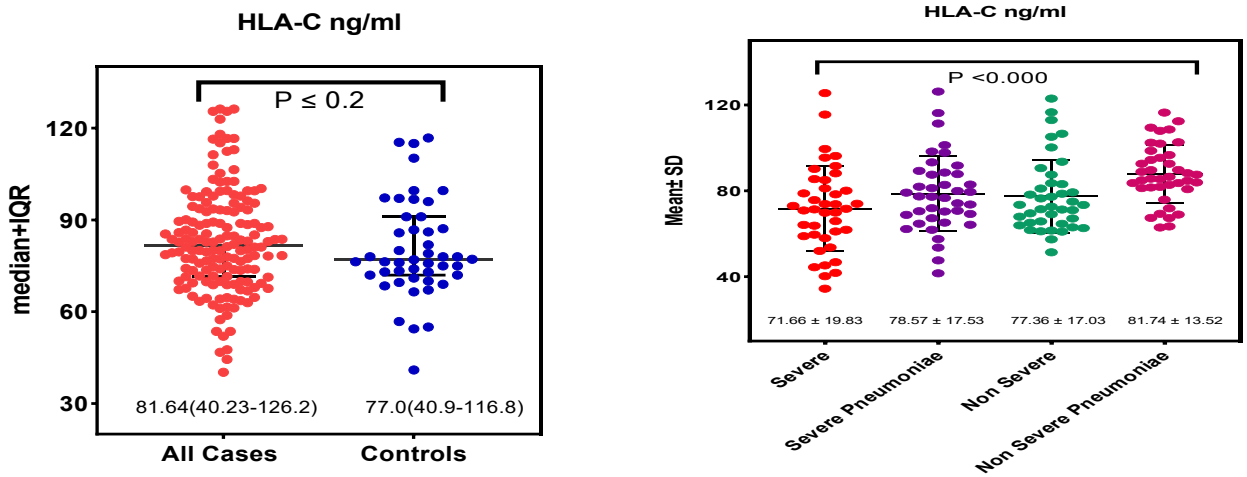

Fig. 1. *Scatter dot plots of HLA-C in all cases of (COVID-19 and Bacterial pneumonia) and healthy controls, and in cases distributed according to the severity of the disease (Horizontal lines indicate medians, while vertical lines indicate interquartile range (IQR). Significant differences assessed with the Mann-Whitney U test (to compare two groups) or the Kruskal-Wallis test (to compare three groups))*

is upregulated in the serum of patients with severe COVID -19. *Human Immunology*, *82*(10), 726–732. https://doi.org/10.1016/j.humimm.2021.07.007

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