Journal of Applied and Natural Science
15(2), 526 - 529 (2023)
ISSN : 0974-9411 (Print), 2231-5209 (Online)
journals.ansfoundation.org

Research Article

Human leukocyte antigen-DRB1 (HLA-DRB1) serum level act as a protective gene among acute respiratory syndrome coronavirus patients

Ruqia Fadhel Habeeb*
Ministry of Health and Environment, Hilla city, Iraq
Noor Salman Khadim Al-Khafaji
Biology Department, College of Science, University of Babylon, Hilla city, Iraq

*Corresponding author. E-mail: ruqiafadhel22@gmail.com

Article Info
https://doi.org/10.31018/jans.v15i2.4395
Received: January 14, 2023
Revised: April, 27, 2023
Accepted: May 3, 2023

How to Cite
Habeeb, R. F. and Al-Khafaji, N. S. K. (2023). Human leukocyte antigen-DRB1 (HLA-DRB1) serum level act as a protective gene among acute respiratory syndrome coronavirus patients. *Journal of Applied and Natural Science*, 15(2), 526 - 529. https://doi.org/10.31018/jans.v15i2.4395

Abstract
Extremely diverse human leukocyte antigen (HLA) genes may contribute in special ways to the immune system's defense against CoV-2 infection caused by SARS. In the present investigation, the human leukocyte antigen was measured levels in the serum (HLA-DRB1). The severity of infection among acute respiratory syndrome coronavirus patients was compared with healthy controls. This case-control study was conducted on 180 acute respiratory syndrome coronavirus patients, including 40 cases of severe corona patients without pneumonia, 40 cases of severe corona patients with pneumonia, 40 cases of non-severe corona patients without pneumonia, 40 cases of non-severe corona patients with pneumonia and 20 cases healthy controls. HLA-DRB1 was identified among four cases and compared to healthy controls. The patients with SARS-CoV-2 had a reduced frequency of HLA-DRB1 when the results using the Kruskal-Wallis analysis were compared. The serum concentration for HLA-DRB1 through individuals with respiratory distress symptoms brought on by viral, and bacterial infections decreased, falling to 38.88 ng/L in severe corona patients without pneumonia, 34.35 ng/L in severe corona patients with pneumonia cases, 46.20 ng/L in non-severe corona patients without pneumonia cases, 51.13 ng/L in non-severe corona patients with pneumonia cases, and 59.95 ng/L in healthy controls (P ≤0.02). HLA-DRB1 was also found at a reduced frequency in all acute respiratory syndrome coronavirus antibody-positive patients compared to controls. The SARS CoV-2 illness and HLA-DRB1 were related and may have protective properties in acute respiratory syndrome coronavirus infection. In addition, DRB1 was associated with protection from SARS-CoV-2 and bacterial infection.

Keywords: Acute respiratory syndrome coronavirus, Human leukocyte antigen (HLA-DRB1), ELSA test

INTRODUCTION

Internationally, around 89 million people have contracted the disease. with coronavirus disease 2019 (COVID-19) yet another year since Wuhan first reported infection with the coronavirus 2 that causes serious acute respiratory symptoms SARS¸CoV-2 (China) (Littera *et al,.*2020). The novel beta coronavirus infection is spreading globally, yet significant regional variations exist. Researchers' the pathogenesis of this viral infection is understood is further hampered by variances changes in the symptoms as well as the intensity of the COVID-19 illness (Debnath *et al.,*2020). Genetic variables linked to disease vulnerability or resistance, particularly those caused by organisms expressed by the human leukocyte ant¡gen (HLÀ) system and located on the shorter arm of chromosome 6 in humans, regulate the immune response against pathogens (Crux *et al.,*2017). The advancement of COVID-19 is believed to be influenced by factors such as host genetics, particularly immune-regulated genes like the human leukocyte antigen (HLA) gene, age, comorbid conditions (such as diabetes, fatness, cardiovascular diseases, and so on), cytokine storm, and conditions that lead to other pathogens (Nguyen *et al.,*2020). Among the many genetic variables linked to SARS-CoV-2 infections, immune-related genes have been postulated to substantially influence COVID-19 susceptibility or resilience, the severity of the disease, and prognosis (Wang *et al.,* 2020). In these instances, individual differences in the immune system's response to a bacterial illness and the SARS-CoV-2 virus are influenced by the HLA genes' extraordinary variety among various cultures (Debnath *et al.,*2020). Given the critical function that

HLA molecules play in bending to viral antigens peptides and presenting them to virus-specific cytotoxic T lymphocytes, HLA alleles, the much more polymorphic genomic structure, may work as susceptible sites or possibly may give protection versus viral diseases (Debnath *et al.,*2020) and (Nguyen *et al.,*2020). The exons that translate for this part of the HLA molecules have genetic code differences that affect the amino acids that are present within the peptide-binding cleft. These variations determine whether the HLA genes are positively or negatively associated with infectious disorders (Nguyen *et al.,*2020) and (Poulton* *et al.,*2020). Monocytes, developed macrophages, dendritic cells, and B cells are examples of antigen-presenting molecules that exhibit the class¸II human leukocyte antigen (HLA) HLA-DR upon the surface of cells. Since the initial description of the involvement of HLA-DRB1*in immunosuppression, HLA-DRB1*presence on monocytes is a reliable marker for evaluating immunological dysfunction and risk of secondary bacterial infection in sepsis and trauma patients (Zhang *et al.,*2021). Consequently, lower HLA-DRB1 levels can also cause COVID -19. This study aimed to identify the serum levels of the human leukocyte antigen (HLA-DRB1) and to compare the severity of infection among acute respiratory syndrome coronavirus patients with healthy controls.

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 dispersed in order of severity as follows: 40 severe without pneumonia,40 severe with pneumonia, 40 non-severe without pneumonia, 40 non-severe with pneumonia, and 20 healthy controls, all groups of COVID-19 patients have positive results for PCR tests and positive results for *Streptococcus pneumoniae* and *Klebsiella pneumoniae* in patients with bacterial infections who have spent two months receiving care at the COVID-19 Centres in Babylon Province's Marjan Medical City and Emam Sadeq Hospital (December 2021 and January 2022). Five ml of venous blood from each person was collected. The skin above the vein was treated with 70% ethanol, which was then placed in a Gel tube to separate the sera. The blood was centrifuged for five minutes at a speed of 3000 rpm after 30 minutes at room temperature. The sera were then split into two repeaters and kept frozen at -20 ^{0}C in a clean Eppendorf tube.

Immunological aspects

Following the manufacturer's protocol, an ELISA kit was used to measure the concentrations of HLA-DRB1 in serum in vitro (Korain Biotech CO.). 16.28 ng/L was the lowest value of detection.

Ethical approval

After receiving the necessary authorization from the government, approvals were gained from all participants. The following facts are noted: Name, Age, Sexual orientation, Infection date, and Chronic illness.

Statistical analysis

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

RESULTS AND DISCUSSION

HLA-DRB1 serum level estimation in COVID-19 patients

The present study examined the severity of the illness among 160 people with acute respiratory syndrome and the prevalence of HLA-DRB1 in comparison to healthy controls. The patient had lesser HLA-DRB1 frequency levels with the coronavirus-induced acute respiratory syndrome, with severe without pneumonia cases having levels of 38.88 ng/L, severe with pneumonia cases having levels of 34.35 ng/L, non-severe without pneumonia cases having levels of 46.20 ng/L, non-severe with pneumonia cases having levels of 51.13 ng/L and controls having levels of 59.95 ng/L (P ≤0.02) as shown in Table 1. In the case of disease severity, HLA-DRB1 levels between patients with Severe without pneumonia, Severe with pneumonia, Non_Severe without pneumonia, or Non-Severe without pneumonia indicate substantial differences (P ≤ 0.001) (Fig. 1). Given that HLA molecules play a crucial role in the activation and production of T cell-mediated antiviral immunity, HLA DR may determine the genetic vulnerability to or potential protection against SARS CoV-2 and they can be linked with the severity, prognoses, and outcome of illnesses (Littera *et al*., 2020) and (Nguyen *et al*.,2020).

Valtierra-Alvarado, M *et al.* (2022) support the findings of the current study, where the patients with type 2 diabetes mellitus (T2DM) showed a reduced frequency of HLA-DRB1. As HLA-DRB1 little cells have been linked to an immunosuppressive phenotype in MDSCs, a rise in the number of these cells may indicate a decline in immunological defenses. By using flow cytometry, the prevalence of healthy controls and T2DM patients' levels of HLA-DR low (negative or low expression of HLA-

Table. 1. Estimation of HLA-DRB1 serum levels among acute respiratory syndrome coronavirus patients

Type of patients	No. of patients	HLA-DRB1 ng/L Mean Rank	P-value
Severe	40	38.88	0.02
Sever Pneumoniae	40	34.35	
Non-severe	40	46.20	
Non-severe Pneumoniae	40	51.13	
Control	20	59.95	

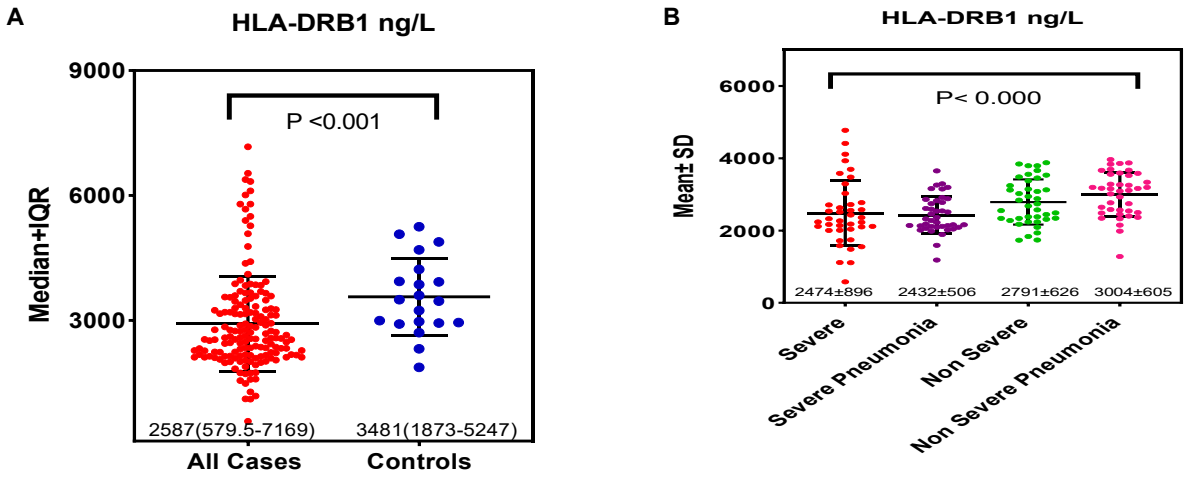

Fig. 1. ***A.*** *Scatter dot plots of HLA-DRB1 in all cases of acute respiratory syndrome coronavirus and healthy controls,* ***B.*** *cases distributed according to the severity of the disease. Horizontal lines indicate medians, while vertical lines indicate interquartile range (IQR). Significant differences were assessed with the Mann-Whitney U test to compare two groups and the Kruskal-Wallis test (to compare three groups).*

DR cells were assessed. To do this, HLA-DR downregulation and the fluorescence minus one (FMO) controls were used to characterize and separate the HLA-DR-/low population.

Restrepo *et al.* (2021) support this finding in all monocyte subsets from diabetic patients' conditions; reduced HLA-DR expression can be seen regardless of dyslipidemia status. While cholesterols, particularly LDL, balance the reductive effect, triglycerides tend to cause depression, and lipids may also affect the expression of the HLA-DR gene.

Domon *et al.* (2021) support the present study and found the treatment of THP1-derived macrophages to culture supernatant from dead neutrophils reduced the expression of the human leukocyte antigen (HLA) class II molecule. Additionally, macrophage extracellular vesicles were isolated, and neutrophil elastase cleaved HLA-DRB1 on those vesicles without causing morphological alterations. Therefore, neutrophil elastase leakage may impair antigen presentation, innate immunological responses, and T-cell activation. Neutrophil elastase inhibition is another potential treatment approach for the management of viral and bacterial pneumonia.

Conclusion

The present study provides evidence that HLA-DRB1 has a preventive effect against bacterial infection and the SARS-CoV-2 virus. It is one of the elements in preventing coronavirus in people with the acute respiratory syndrome.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Crux, N. B. & Elahi, S. (2017). Human leukocyte antigen (HLA) and immune regulation: How do classical and non-classical HLA alleles modulate immune response to human immunodeficiency virus and hepatitis C virus infections? *Frontiers in Immunology*, 8, 8,832.https://doi.org/10.3389/fimmu.2017.00832.
2. Debnath, M., Banerjee, M. & Berk, M. (2020). Genetic gateways to COVID-19 infection: Implications for risk, severity, and outcomes. *FASEB Journal*, *34*(7), 8787–8795-8795.https://doi.org/10.1096/fj.202001115R.
3. Littera, R., Campagna, M., Deidda, S., Angioni, G., Cipri, S., Melis, M., Firinu, D., Santus, S., Lai, A., Porcella, R.,

Lai, S., Rassu, S., Scioscia, R., Meloni, F., Schirru, D., Cordeddu, W., Kowalik, M. A., Serra, M., Ragatzu, P., . . . & Chessa, L. (2020). Human leukocyte antigen complex and other immunogenetic and clinical factors influence susceptibility or protection to SARS-CoV-2 infection and severity of the disease course. The Sardinian experience. *Frontiers in Immunology*, *11*, 605688, 605688. https://doi.org/10.3389/fimmu.2020.605688.

4. Domon, H., Maekawa, T., Isono, T., Furuta, K., Kaito, C. & Terao, Y. (2021). Proteolytic cleavage of HLA class II by human neutrophil elastase in pneumococcal pneumonia. *Scientific Reports*, *11*(1), 1-9. https://doi.org/10.1038/s41598-021-82212-5.
5. Nguyen, A., David, J. K., Maden, S. K., Wood, M. A., Weeder, B. R., Nellore, A. & Thompson, R. F. (2020). Human leukocyte antigen susceptibility map for severe acute respiratory syndrome coronavirus 2. *Journal of Virology*, *94*(13), e00510-20. https://doi.org/10.1128/JVI.00510-20
6. Poulton, K., Wright, P., Hughes, P., Savic, S., Welberry Smith, M., Guiver, M., Morton, M., van Dellen, D., Tholouli, E., Wynn, R. & Clark, B. (2020). A role for human leucocyte antigens in the susceptibility to SARS□Cov□2 infection observed in transplant patients. *International Journal of Immunogenetics*, *47*(4), 324–328-328. https://doi.org/10.1111/iji.12505.
7. Restrepo, B. I., Twahirwa, M. & Jagannath, C. (2021). Hyperglycemia and dyslipidemia: Reduced HLA-DR expression in monocyte subpopulations from diabetes patients. *Human Immunology*, *82*(2), 124–129-129. https://doi.org/10.1016/j.humimm.2020.11.005.
8. Valtierra-Alvarado, M. A., Castañeda-Delgado, J. E., Lugo -Villarino, G., Dueñas Arteaga, F., Rivas-Santiago, B., Enciso-Moreno, J. A. & Serrano, C. J. (2022). Increased frequency of CD14+ HLA-DR−/low cells in type 2 diabetes patients with poor glycemic control. *Human Immunology*, *83*(11), 789–795-795. https://doi.org/10.1016/j.humimm.2022.08.011.
9. Wang, F., Hou, H., Yao, Y., Wu, S., Huang, M., Ran, X., Zhou, H., Liu, Z. & Sun, Z. (2020). Systemically comparing host immunity between survived and deceased COVID-19 patients. *Cellular and Molecular Immunology*, *17*(8), 875–877-877. https://doi.org/10.1038/s41423-020-0483-y.
10. Zhang, L., Li, R., Song, G., Scholes, G. D. & She, Z. S. (2021). Impairment of T cells' antiviral and anti-inflammation immunities may be critical to death from COVID-19. *Royal Society Open Science*, *8*(12), 211606 , .211606 https://doi.org/10.1098/rsos.211606.