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COVID-19 in systemic lupus erythematosus; a mini-review on current knowledge

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Abstract
The consequences of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection vary among persons, while some individuals are at high risk. Patients with systemic lupus erythematosus (SLE) and COVID-19 necessitate particular attention. SLE cases may be at particular risk for SARS-CoV-2 due to their dysregulated immune system and immunosuppressive treatments. Organ injury and administration of systemic glucocorticoids and other immunosuppressive agents are the risk factors for severe SARS-CoV-2. Additionally, SLE is not uncommon and could be severe in some ethnicities like African and Hispanic individuals and may be accompanied by poor outcomes of SARS-CoV-2. Thus, knowledge of the triggering immune response and therapeutic modalities in SLE and SARS-CoV-2 is necessary to guide treatment of this serious infectious disease in the background of SLE and vice versa.

Keywords: Systemic lupus erythematosus, COVID-19, SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2, Cytokine release syndrome, Immunosenescence
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Introduction

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection, is presented as a mild to moderate disease in most previously healthy persons; however, it can cause a life-threatening condition in some individuals (1).

Structurally, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a RNA base genome can cause coronavirus disease 2019 (COVID-19). This infection is exceedingly contagious and has a high mortality rate in some particular conditions (2). Various pathophysiological features like pulmonary and extra-pulmonary disease, and also immune related mediators such as cytokine overproduction, make the clinical features of this disease. Among the contributed factors, the immune reaction to SARS-CoV-2, has a soft balance between defensive processes and injurious pathological consequences (3). In this updated mini-review, we aimed to study the most recent investigation on the impact of COVID-19 on systemic lupus erythematosus (SLE) as an autoimmune disease. In SLE, baseline immune outlines and their alteration throughout initial acute infection may be critical to predict the period of this disease. This review may help to conceive better attention to immune monitoring modalities for SARS-CoV-2, comprising various tools to guess disease activity and severity too (3).

Methods

For this narrative review study, related articles were searched in Scopus, Embase, EBSCO, Web of Science and Google Scholar and also in PubMed/Medline. The following search terms such as systemic lupus erythematosus, SLE, coronavirus disease 2019, COVID-19, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2, cytokine release syndrome and immunosenescence were utilized to retrieve the published articles on this subject.

Auto-immunity in infection disease

Infectious diseases have been long detected as one of stimulators for auto-inflammatory and autoimmune syndromes, principally by molecular imitation (4). Cytokine release syndrome with diminished number of peripheral white blood cells, along with functional overtiredness of defensive cells particularly T-cells has been recognized as undesirable parameters in COVID-19 patients. Severe SARS-CoV-2 infection can represent a condition of immune senescence. Immunosenescence is described as age-related changes of immune system resulting in an extensive lessening in capacity to stimulate active antibody production (5). Further, chronic low-grade infection initiated with aging, named inflammaging, is a predictable parameter for comorbidities for severe cases of SARS-CoV-2. Inflammaging is the result of chronic micro-

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Implication for health policy/practice/research/ medical education

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stimulation of the innate immune system in the elderly which is a damaging process for the immune system (6). In the process of inflammaging, there is also-cell senescence, which is dysfunction of T-cells that happens in chronic infections (7-9). Several reports have been published which showed coronavirus disease 2019 may result in various inflammatory multi-systemic syndrome, which comprises macrophage activation syndrome, Kawasaki disease shock syndrome, Kawasaki-like disease, and myocarditis in pediatric COVID-19 cases (10). Primary investigation showed, through the ACE2 receptor, SARS-CoV-2 enters several organs like liver, testes, intestine, lungs, kidney and heart. The targeted cells for SARS-CoV-2 is a membrane protein S-protein (spike protein) present on the surface of the pathogen joins to the ACE2 receptor mediated by the transmembrane protease serine 2 (cellular protease TMPRSS2) and by clathrin through endocytosis (11). After viral invasion, the immune system begins to eradicate the virus from the cells, while the body is not capable to regulate the elimination process always. Since the over-activation of immune system eventually results in a hyper-inflammatory phase of SARS-CoV-2 termed cytokine storm syndrome too (12).

Auto-immunity and COVID-19

It is possible that the virus triggers a dysregulated immune reaction and results in initiating the autoimmunity (13). The consequences of SARS-CoV-2 infection vary among people since some individuals are at high risk. Notably, patients with SLE and COVID-19 require particular attention (14). SLE cases may be at particular risk for SARS-CoV-2 due to their dysregulated immune system and immunosuppressive treatments. Organ injury and administration of systemic glucocorticoids and various immunosuppressive agents are risk factors for severe SARS-CoV-2. SLE is not uncommon and could be severe in some ethnicities like African and Hispanic individuals and may be accompanied by poor outcomes of SARS-CoV-2 (15).

There are few published articles on the association of SARS-CoV-2 with SLE, while other reports have shown the link between this infection with some other autoimmune diseases like rheumatoid arthritis and multiple sclerosis. It is possible that SARS-CoV-2 is capable of triggering rheumatoid arthritis (13).

Systemic lupus erythematosus and COVID-19

Systemic lupus erythematosus is an autoimmune syndrome regarded as the disturbing tolerance to nuclear self-antigens and consequently the creation of various autoantibodies (17). This disease involves mainly women with higher rate of mortality in young females (18). Individuals with SLE are counted as susceptible patients for COVID-19. In SLE, an aberrant immune response is considered by the emergence of aberrant T cells, and pro-inflammatory cytokines, circulating autoantibodies, lymphopenia, alongside disturbed immune mechanisms which direct to immune-mediated injury of tissues. Patients with SLE are frequently under treatment with various immune-suppressive agents, which make them be immune-compromise. Therefore, these patients are more vulnerable to infections like COVID-19 (19), though a link between COVID-19 and SLE is not well-defined (20). COVID-19 causes an intense immune provocation in response to the virus, since SARS-CoV-2 raises macrophage inflammatory protein-1 alpha, interferon gamma, tumor necrosis factor-α, IL-6, IL-7, IL-2, IL-10, in patients, that present a feature of macrophage activation syndrome or a secondary hemophagocytic lymphohistiocytosis. Furthermore, acute infection with SARS-CoV-2 can create various autoantibodies, like antinuclear antibodies. Recently, a case of SLE related to a new COVID-19 case was described too (20). We also recently presented a case of aggravation of an undetected pre-existing lupus nephritis subsequent COVID-19 vaccination (21). The relapse of lupus nephritis in our case is probably relegated to SARS-CoV-2 vaccine (21). To evaluate COVID-19 IgG antibody reactivity in SLE individuals, Saxena et al conducted a multi-ethnic, multi-racial investigation. They studied 329 SLE individuals, of them 94% were women and 28% were Hispanic ethnicity, with 16% positivity for COVID-19 IgG. They found, Hispanic ethnicity was more likely to be seropositive patients. The demographic variables and SLE-specific biomarkers, and also immunosuppressant medications had no relationship with SARS-CoV-2 positivity. They found the majority of SLE patients with confirmed SARS-CoV-2 were capable to create and maintain a serological activity in spite of immunosuppressive treatments. This study is certainty regarding the effectiveness and strength of humoral immunity against COVID-19 (22). In spite of a previous report on a modest strengthening in morbidity in SLE patients with COVID-19, a recent study, showed that the incidence of SARS-CoV-2 may be like the general population (23). More recently, a Denmark nationwide cohort investigation to find the frequency of SARS-CoV-2 hospitalization for patients with SLE versus the general population was investigated. This study showed, 16 of the 2533 SLE individuals were hospitalized with SARS-CoV-2 infection. They demonstrated individuals with SLE were at increased risk of hospitalization with COVID-19 (24). The abnormal clotting tendency in both COVID-19 and SLE prone individuals with both diseases, which requires further checking for thrombosis (19). Systemic lupus

erythematosus is characterized by joint inflammation skin manifestation; however, inflammation may involve almost any organ directing to cell damages. There is no definitive for lupus since corticosteroid therapy is frequently essential to control the disease. Systemic lupus erythematosus patients are commonly under treatment of immunosuppressive drugs and cytotoxic agents to manage dysregulated immune function and are immunocompromised and more vulnerable to infections (19).

Conclusion

The immune response is a crucial factor in COVID-19, which determines the body defense, disease extension, seriousness, and clinical outcomes. Systemic lupus erythematosus affects several body organs, which are risk factor morbidity and mortality of COVID-19 in these patients. To monitor COVID-19, from the perspective of SLE, identifying immune reactions is essential for effective management. Thus knowledge on the triggering immune response and therapeutic modalities in SLE and SARS-CoV-2is necessary to guide treatment of this serious infectious disease in the background of SLE and vice-versa.

Authors' contribution

Conceptualization: HN; Methodology: HN and MR; Validation: HN; Formal Analysis: MR & HN; Investigation: MR and HN; Resources: YR; Data Curation: HN; Writing—Original Draft Preparation: MR; Writing—Review and Editing: HN and YR; Visualization: HN; Supervision: HN; Project Administration: HN and MR.

Conflicts of interest

The authors of this mini-review are working in Nickan Research Institute. However, the process of peer-review was no affected by their job.

Ethical issues

The authors have entirely observed ethical issues (including plagiarism, data fabrication and double publication).

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