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Original Article

The frequency of autoimmune diseases among patients with COVID-19 infection

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Abstract

Background There is a hypothesis saying that autoimmune diseases are protective against infections and tumors. The present study is trying to test this hypothesis in regards to COVID-19 infection.

Objective This study aims to collect all patients with COVID-19 and to study the frequency of all autoimmune diseases among these patients and to be compared with their frequency in the general population.

Methods This is case series descriptive observational study where all patients with COVID-19 infections had mild to moderate infections. They are all PCR positive and demographic features were registered. Also, patients were screened and examined for any cases of autoimmune diseases.

Results A total of 125 patients with COVID-19 infection were evaluated with an age range from 16-85 years with a mean±SD of 41.68±15.12 years, with 67 (53.6%) females and 58 (46.4%) males. The frequency of the following autoimmune diseases (AD) was found and as follows: Psoriasis in 17(13.6%) cases, vitiligo 10(8%), alopecia areata 6(4.8%), lupus erythematosus 4 (3.2%), pemphigus one (0.8%). When these figures for ADs compared with figures in the general population, they had statistically significantly no protection against COVID-19 infection but on contrary, they had increased risk to get the infection and in descending order: psoriasis, alopecia areata, pemphigus, vitiligo, and lupus erythematosus.

Conclusion The hypothesis of autoimmune diseases is protective against infections is not valid for patients with psoriasis, alopecia areata, pemphigus, vitiligo, and lupus erythematosus but on contrary, they had an increased risk to get COVID-19 infection.

Key words
COVID-19, pemphigus, vitiligo, alopecia areata, lupus erythematosus and psoriasis.

Introduction

SARS-Cov-2 (COVID-19) has infected over 139.5 million individuals with approximately a 2.14 per cent mortality rate.[1,2] Individuals with autoimmune disorders (AD) are considered to be at increased risk of contracting infectious diseases.[3] However, AD patients have been shown to be less likely to test positive for SARS-Cov-2 at the time of pandemic. Misinterpretation of this and other data can lead to the spread of inaccurate information suggesting that ADs are protective against SARS-Cov-2.[4] This study hence seeks to highlight the current data on SARS-Cov-2 and AD association to provide clarity for physicians and the general population.

The primary argument for autoimmune diseases

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being protective is that lower numbers of individuals with ADs have been shown to test positive for SARS-Cov-2 than incidence numbers for the general population would predict.[4] As AD patients are often treated with immunosuppressant, they are in a higher risk category for respiratory infections with symptoms similar to those of SARS-Cov-2, that is, coughing and fever.[5] Historically, AD patients have been at risk of more severe symptoms during influenza infection[6] and are more likely to be hospitalised due to infections.[3,7] This led to the hypothesis that AD patients have a higher risk of catching viruses. In the case of SARS-Cov-2, this does not seem to be the issue. In fact, AD patients are not at additional risk of contracting SARS-Cov-2 compared to the general population.[8] Therefore, in the case of the SARS-Cov-2 virus, AD patients have better protection against this infection compared with other viruses, but are not necessarily more protected than the general population.

One reason for this could be the immunomodulatory drugs used by AD patients. Tocilizumab, an anti-rheumatic immunosuppressive drug, is effective in reducing the likelihood of disease progression.[9] Likewise, corticosteroid therapy is also currently used to reduce disease progression.[10] Corticosteroids were initially suggested to cause serious infection risks,[11] but as they are seemingly beneficial when focusing specifically on therapy and they appear useful. AD patients treated with specific drugs could hence be more protected against SARS-Cov-2, but this benefit would also likely be applicable for non-AD SARS-Cov-2 patients, so any protectiveness would not be associated with the ADs themselves.

Another important consideration of the potential AD protectiveness against SARS-Cov-2 is whether AD patients have more or less severe complications, hospitalisations and outcomes compared to the general public. Murtas *et al*.[4] found no difference in disease prognosis between AD and non-AD patients. Supporting this, one study evaluated the severity of SARS-Cov-2 symptoms in patients with chronic arthritis treated with immunosuppressive drugs. Although not compared to the general population, the results did not show any correlation between the diseases and severe symptoms.[12] Another study assessed two groups of SARS-Cov-2-positive patients; the first group had no ADs, whereas the other with ADS and was on immunomodulatory drug treatment. It was observed that some symptoms linked to COVID-19, such as loss of smell and taste, dyspnoea and weakness, were higher in the immunologically treated patients. However, this study did not find any significant differences between both groups regarding hospitalisation and mortality.[13] On the other hand, studies performed by Pablos *et al*.[14] and Grasselli *et al*.[15] showed that patients with ADs were more likely to be hospitalised because of SARS-Cov-2. Therefore, evidence surrounding disease severity currently is conflicting and requires more data.

Due to the recent appearance of the virus SARS-Cov-2, the information obtained to date is scarce and sometimes contradictory. Although several studies have been performed since the first SARS-Cov-2 outbreak, the lack of information and the still on going and evolving nature of the pandemic do not allow definitive results to be obtained. So far, no conclusive data are showing that ADs confer either protection against or susceptibility to the SARS-Cov-2 infection compared to the general population. Nevertheless, some studies show a possible link between AD patients and a higher risk for respiratory infections in general, but no specific risk factor for SARS-Cov-2 has been identified.[4] Currently, AD medications, such as tocilizumab,

are being used as a treatment for SARS-Cov-2; this may provide the most reasonable explanation for any protective role that ADs have against the SARS-Cov-2 infection.

Although any SAR-Cov-2 protection may be related to ADs medications rather than the ADs themselves, there are many studies that support the idea that patients with autoimmune skin diseases have protection against skin infections and tumours, especially when compared with the general population. Sharquie *et al*. have published several articles showing that autoimmune diseases such as pemphigus, vitiligo, alopecia areata and systemic lupus erythematosus and psoriasis[16] confer protection against skin infections including viral infections and tumours, even though these diseases are managed with immunosuppressive drugs as part of a prolonged course of therapy.[17] For example, pemphigus vulgaris patients, although on a long course of immunosuppression, are protected against skin infections and skin tumours, whereas kidney transplant recipients, also on immunosuppressive drugs, are not protected,[17] thus the protective effect cannot be solely attributed to the drugs.

Likewise, vitiligo has protective factors against the development of skin tumours, infections and photosensitivity, and the absence of melanin from the epidermis is not a significant risk factor for the development of skin tumours.[18] So, vitiligo has been causally associated with lower risk factors for many cancers, suggesting that vitiligo as an autoimmune disease might play a role in the suppression of cancer.[19] As it has been found that marker p53 is overexpressed in vitiliginous skin compared with both the adjacent skin and healthy skin as a control group, this can partially explain the protection against skin malignancies.[20] Also, it is well documented that severe vitiligo and alopecia areata are more protective against infection compared with milder versions of these diseases. This protection is also more intense in the following diseases: pemphigus, vitiligo, alopecia areata and SLE and psoriasis as listed in decreasing order of protection.[21]

The frequency and percentages of these ADs among general populations vary in different geographical locations but generally are around 2% in vitiligo,[22] alopecia areata,[23] and psoriasis.[24] As regard lupus erythematosus is around 0.053% in SLE[25] and 0.025% for DLE[26] and for both together around 0.0394%.While in pemphigus around 0.00185%.[27,28]

All of these studies provide supporting evidence that autoimmune diseases and those with autoimmune reactions confer better protection against infections in general, and this could be extended to include the COVID-19 infection. Thus, the objective of the present work is to find the frequency of these autoimmune diseases occurrence in patients with COVID-19.

Patients and methods

This is case series descriptive observational study where all patients with covid-19 infections were registered during the period from Jan 2021 to May 2021.They all had mild to moderate infections and were treated at home and no need for hospital admission. They are all polymerase chain reaction (PCR) positive and demographic features were registered. Also patients were screened and examined for any case of autoimmune disease that appeared before infection or after. The frequency of these disease was compared with frequency percentages among general populations to have the degree of significance. Formal ethical approval was obtained from all patients.

Statistical analysis

Calculations were performed using Microsoft

Excel version 2013. Categorical variables were expressed in frequency and percentages, continuous variables presented as (mean±standard deviation). Chi-square was used to assess the significance of the relationship between two categorical variables. P-value with numbers ≤0.05 was considered statistically significant.

Results

A total of 125 patients with COVID-19 infection were evaluated 1-2 months after recovery from infection, with age range from 16-85 years with a mean±SD of 41.68±15.12 years, with 67(53.6%) females and 58 (46.4%) males. All ADs were present before COVID-19 infection but only one patient with psoriasis where illness appeared after infection. The frequency of the following AD diseases was found and as follow: Psoriasis in 17 (13.6%) cases, vitiligo 10 (8%), alopecia areata 6 (4.8%), lupus erythematosus (2 cases DLE and 2 cases SLE) 4 (3.2%), pemphigus one (0.8%) case. When these compared with figures in general population, they all had statistically significantly no protection against COVID-19 infection but on contrary they had increased risk to get the infection and in descending order psoriasis, alopecia areata, pemphigus, vitiligo and lupus erythematosus as shown in **(Table 1)** and patients with psoriasis had the highest risk to get COVID-19 infection.

Discussion

Autoimmune diseases (AD) occur commonly as affecting around 5% of general population worldwide[29,30] and they arise when immune responses mounted in the host are directed against self-components with consequences loss of self-tolerance and that followed by immune destruction of host tissues. All these ADs are common skin diseases where there is immune reaction against normal tissue, resulting in destruction of cells, thus ending in a disease state like pemphigus, vitiligo, alopecia areata, lupus erythematosus, psoriasis and others.31 These ADs had been shown by many studies to provide protections against infections and tumors and in decreasing orders **(Figure 1)** and the most protective disease was vitiligo and the least protective was psoriasis.[16,22-25]

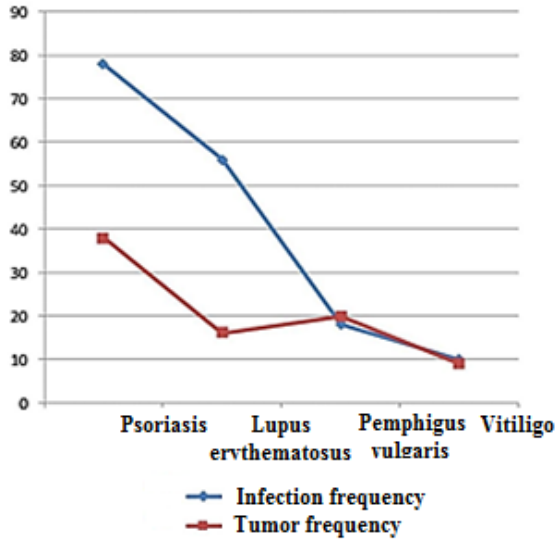

Figure 1 Comparison of frequencies of autoimmune diseases like psoriasis, lupus eythematosus, pemphigus and vitiligo [16].

Table 1 Distribution of autoimmune diseases in general population and in patients with COVID-19 infection.

	Disease	*AD percentage in COVID-19 group*	*AD percentage in General Population*	*Chi-Square*	*P-value*	*OR At 95% CI*
1	Psoriasis	13.6	2	162	<0.000001	9.43
2	Alopecia areata	4.8	2	17.4	=0.000029	3.6
3	Pemphigus	0.8	0.00185	14.86	=0.0001	84.
4	Vitiligo	8	2	11.1	=0.0008	16
5	Lupus Erythematosus	3.8	0.094	8.72	=0.0031	7.3

OR= Odds Ratio, 95% CI= Confidence Interval.

The frequencies of these different ADs among general populations are around 2% for vitiligo, alopecia areata and psoriasis, while for lupus erythematosus around 0.0394% and pemphigus around 0.00185%.

While the frequency of these diseases among patients with COVID-19 infections as had been shown in the present work were as follow; psoriasis 13.6%, vitiligo 8%, alopecia areata 4.8%%, lupus erythematosus 3.2%, and pemphigus 0.8%. These figures are much higher than those seen in clinical practice and in general population and are statistically significantly high.

When these diseases compared with each other, the following ADs and in descending orders are the more risky to get COVID-19 infection like psoriasis, alopecia areata, pemphigus, vitiligo and lupus erythematosus respectively. So psoriasis and vitiligo have a high risk to get infection as these two diseases are considered close relative and twin of one disease.[32]

Hence we can conclude that these ADs do not give protection against covid-19 infection on contrary to what had been published where these diseases like vitiligo, pemphigus, alopecia areata, lupus erythematosus and psoriasis confer protection against infections and tumors.

The reason behind this discrepancy and these controversial results could not be well explained but we can speculate that covid-19 virus is still a strange virus that does not follow the rules and behaviour of other viruses, hence the self-immune reactions in these ADs might help the entry of COVID-19 virus into cells rather than do protection. Further discussion, suggestion and studies are highly recommended to support the present observation and to find explanation for these odd results.

Conclusion

The results of current study had shown autoimmune diseases like psoriasis, alopecia areata, pemphigus, vitiligo and lupus erythematosus do not confer protection against COVID-19 infection but on contrary they had increased the risk to get this infection. The reason behind this discrepancy could not be explained at the time being and further investigative studies are highly needed.

Limitations

The limitation of this study as the results are confined to patients with COVID-19 infection rather than compared with healthy control.

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