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Evaluation of the alopecia areata patients on tofacitinib treatment during the COVID-19 pandemic

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Abstract

Tofacitinib is a Janus Kinase 3 inhibitor that is used in the treatment of alopecia areata. We recommended our alopecia areata patients to discontinue their tofacitinib treatment during the COVID-19 pandemic for an average of 80 days. We aimed to evaluate the drug use and the SARS-CoV-2 infection status of alopecia areata patients; and the relationships of recurrence to age, gender, treatment duration, and tofacitinib discontinuation. One-hundred and ninety-one (61.4%) patients were off the drug and 120 (38.6%) were on therapy during the pandemic. The relationship between drug discontinuation due to the COVID-19 pandemic and recurrence was statistically significant ($P < .001$). Statistically significant relationships of age ($P = .013$) and treatment duration ($P < .001$) to recurrence were also found. The change in the SALT score differed between the patients on therapy and off therapy during the pandemic ($P < .001$). A significant negative correlation was found between the change in the SALT score and treatment duration: the spearman correlation test $P = .018$. We concluded that the patients may continue to the tofacitinib therapy during the rest of the COVID-19 pandemic if the benefit outweighed the risk.

KEYWORDS
alopecia, areata, covid, pandemic, tofacitinib

1 | INTRODUCTION

Alopecia areata is a nonscarring alopecia, which can be aggravated by psychological stress. Autoimmunity has an important role in the pathogenesis of the disease. Janus Kinase 3 (JAK-3) hyperactivity has a key role in the disease pathogenesis; JAK-1 and JAK-2 hyperactivity contribute to a lesser extent.[1,2] Tofacitinib is a nonselective JAK inhibitor which has been used in the treatment of alopecia areata. The drug is frequently discontinued during viral infections since it causes immunosuppression.[3] Long-term use of tofacitinib was shown to be effective in achieving low-SALT scores with long-term remission in a large series.[1]

The COVID-19 pandemic began in December 2019. The course of the disease is more severe in elderly patients with cardiac cormorbities, and in hypertensive and diabetic patients. Immunosuppressed patients also have a more severe course.[4] Due to the unknown course and high mortality rate of the disease, we recommended our patients to discontinue immunosuppressive drugs, including tofacitinib, during the pandemic. This study aims to evaluate the drug use and the SARS-CoV-2 infection status of alopecia areata patients; and the relationships between recurrence, age, gender, treatment duration, and tofacitinib discontinuation. Thus, by way of this study, we aim to validate the use of tofacitinib in alopecia areata patients in the ensuing course of the pandemic.

2 | MATERIAL AND METHOD

2.1 | Study design

This is a retrospective study evaluating the tofacitinib use in alopecia areata patients during the COVID-19 outbreak. All of the patients who were diagnosed with alopecia areata and were currently receiving tofacitinib in the Istanbul University-Cerrahpaşa, Cerrahpaşa

Medical Faculty Dermatology Department Hair Diseases Outpatient Clinic before the COVID-19 outbreak were included in this study. Under normal circumstances, tofacitinib therapy (2 x 5 mg) is given along with biotin supplementation 2 x 2.5 mg/day. During the pandemic, tofacitinib was recommended to be discontinued and the patients only received biotin supplementation. The age and gender of the patient, duration of the tofacitinib therapy, drug use during the outbreak, whether or not the patient had been infected with SARS-CoV-2, the recurrence status and the change in the SALT score during the pandemic of each patient were noted. The approval of the Cerrahpaşa Medical Faculty Ethics Committee was taken (10/09/2020-117 837).

2.2 | Statistical analysis

The SPSS version 21 was used in the statistical analysis. The Kolmogorov Smirnov test was used in the evaluation of the continuous variables. The Pearson chi-square test and Mann-Whitney *U* tests were used in the comparison of the groups. A *P*-value less than .05 was accepted as being statistically significant.

3 | RESULTS

A total of 311 patients were included in this study; 150 (48.2%) of these patients were male and 161 (51.8%) were female. The mean age of the patients was 31.68 years with a SD of 14.32 years. The mean age of the patients who discontinued the therapy was 33.03 years, while the mean age of the patients who were on therapy during the pandemic was 29.0 years. The mean treatment duration was 12.11 months with a SD of 10.92 months. The shortest treatment duration was 1 month and the longest was 52 months. Of all the patients, 191 (61.4%) discontinued the drug due to COVID-19 pandemic and 120 (38.6%) were on therapy. The average duration of the tofacitinib discontinuation during the COVID-19 outbreak was 80 days. Only 1 (0.3%) patient was diagnosed with COVID-19.

One-hundred and sixty-six patients (53.4%) had recurrence during the COVID-19 outbreak. The percentage change in the SALT score in all the patients was 7.76; the percentage change in the SALT score in the patients suffering of recurrence during the COVID-19 pandemic was 20.65. One-hundred and forty-five patients (46. %) did not have any recurrence during the COVID-19 outbreak; 166 (53.4%) had recurrence during the COVID-19 outbreak. Eight of the patients who had recurrence were on therapy during the outbreak, and 158 of the patients with recurrence had discontinued the drug due to the COVID-19 pandemic. The results are summarized in Table 1.

The relationship between drug discontinuation due to the COVID-19 pandemic and recurrence was found to be statistically significant ($P < .001$); the disease recurred more when tofacitinib therapy was discontinued due to outbreak as opposed to when on therapy. A statistically significant relationship between age and recurrence was found ($P = .013$); alopecia areata recurred more in older patients upon the discontinuation of tofacitinib therapy during the COVID-19 pandemic. Again, a statistically significant relationship between the treatment duration and recurrence during the pandemic was found ($P < .001$); alopecia areata recurred less in patients with prolonged drug use upon discontinuation of tofacitinib therapy due to the COVID-19 outbreak. A statistically significant difference in the change in the SALT score was found between the patients on therapy and off therapy during the pandemic ($P < .001$). Furthermore, a significant negative correlation was found between the change in the SALT score and treatment duration: Spearman correlation test $P = .018$; that is recurrence occurred to a lesser extent during the COVID-19 pandemic in patients with longer treatment duration. There was not a statistically significant relationship between gender and recurrence during the pandemic ($P = .64$).

4 | DISCUSSION

In this study, we found that the recurrence of alopecia areata during the COVID-19 pandemic was statistically significantly more in patients who discontinued tofacitinib than in those who continued with therapy ($P < .001$). The severity of recurrence, which was evaluated with the change in the SALT score, was more in patients off-therapy during the COVID-19 outbreak ($P < .001$). Previously, Guo et al reported in their meta-analysis that there is an overall 24% recurrence rate in alopecia areata for tofacitinib therapy and that most of the recurrences occurred upon the discontinuation of therapy.[5] Psychiatric stress is a known exacerbating factor for alopecia areata.[6] COVID-19 pandemic was a major stress inducer for public health.[7] The disease recurrence during the COVID-19 pandemic was not only due to the discontinuation of tofacitinib, but also due to increased stress. Nonetheless, recurrences were more severe in the off-therapy group during the COVID-19 pandemic as was shown in this study. Only one of the patients who was on therapy during the COVID-19 pandemic suffered from a mild SARS-CoV-2 infection without complications. Therefore,

TABLE 1 Comparison of the patients on and off therapy during the pandemic

	All patients	On therapy	Off therapy
Number	311	120	191
Mean age (years)	31.68	29.0	33.0
Gender (F/M)	161/150	64/56	97/94
Treatment duration (months)	12.11	17.85	8.50
Recurrence (%) ($P < .001$)	53.4	6.7	82.7

we recommend that tofacitinib therapy is continued during the rest of the COVID-19 pandemic as the benefit outweighs the risk since the future duration of the pandemic is still unknown.

This study revealed that recurrence due to tofacitinib discontinuation during the COVID-19 pandemic was observed more in older patients than in younger ones (P = .013). The previous literature search revealed only one study regarding the tofacitinib response in alopecia areata patients according to age. Lucy et al did not find a statistically significant relationship between the age of the patient and response to tofacitinib.[8] There are no previous studies evaluating the relapse rate after tofacitinib discontinuation according to age groups; ours is the first study to evaluate such a relationship. The SARS-CoV-2 infection has a more severe course in older individuals and the fatality rate increases with increased age.[9] Even though recurrence rates are higher in older patients, the discontinuation of tofacitinib therapy during the COVID-19 pandemic is a plausible option regarding the increase in mortality with increased age.

This study revealed that recurrence rates after the discontinuation of tofacitinib therapy due to the COVID-19 pandemic were lower in patients with prolonged drug use (P < .001). Similarly, the changes in the SALT scores were less in patients on a longer treatment duration than in shorter ones upon tofacitinib discontinuation due to the COVID-19 pandemic (P = .018). There are previous reports of increased hair shedding after tofacinib and ruloxitinib (which is also a JAK inhibitor) discontinuation. However, none of the reports evaluated the relationship of the relapse rate with the treatment duration.[10,11] Considering our results, the discontinuation of tofacitinib therapy due to the COVID-19 pandemic, if it continues, is safer in terms of the recurrence in patients with prolonged treatment durations than those with shorter therapeutic periods. Thus, the drug may be discontinued due to the COVID-19 pandemic in patients with prolonged therapeutic durations when it is necessary due to the age or comorbid diseases of the patient.

The COVID-19 pandemic has not only changed every day dermatologic practice, but also it has changed the management of autoimmune diseases requiring immunosupressive therapy.[12] Tofacitinib is long known to increase viral infections due to its immunosupressive effects.[3] As a result, we recommended our patients to discontinue tofacitinib during the COVID-19 pandemic for several months. Recurrence was more frequently observed in patients who discontinued the drug due to the pandemic. Furthermore, older patients and patients who have received therapy for a shorter time period showed a greater increase in the SALT score. Only one of our patients had been infected with SARS-CoV-2. The future duration of the pandemic is still unknown. Thus, we recommend that patients continue on tofacitinib therapy during the rest of the COVID-19 pandemic when the benefit of tofacitinib therapy outweighs the risk.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

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