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ASSOCIATION BETWEEN ALOPECIA AREATA AND COVID-19: A SYSTEMATIC REVIEW

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Abstract

Objective: *Alopecia areata (AA) is an inflammatory condition that damages hair cells and causes hair thinning. COVID-19-induced cytokine shift, antigen mimicry between the virus and hair follicles, and COVID-19-induced tissue destruction that revealed autoantigens. This study aims to review the existing literature systematically.*

Materials and methods: *A systematic search strategy was conducted across several electronic reference databases (PubMed, Cochrane Library, ProQuest) and included articles published between 2020–2023. Duplicate publications, review articles, and incomplete articles were excluded.*

Results: *Database search yielded a total of 287 articles, which were systematically eliminated, leaving 6 relevant articles. Analyzed articles showed the incidence of alopecia areata (hair loss) in patient post-COVID-19.*

Conclusion: *COVID-19 is a disease that has very wide clinical manifestations. The mechanism of association between COVID-19 and alopecia areata is unclear. However, several factors can also have an effect, such as race, age, and gender.*

Keyword: *alopecia areata; covid-19; hair loss*

INTRODUCTION

A new human contagious illness called coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2 coronavirus, first discovered in Wuhan, China, in December 2019. The World Health Organization (WHO) proclaimed a worldwide emergency and pandemic for COVID-19 on January 30, 2020, and March 11, 2020, respectively.[1] From asymptomatic forms to serious viral pneumonia with respiratory failure, multiorgan and systemic dysfunctions in sepsis and septic shock, and mortality, COVID-19 has shown a broad range of clinical symptoms.[2,3]

Alopecia areata (AA) is an inflammatory condition that damages hair cells and causes hair thinning. There are many different trends and degrees of seriousness for hair loss.[4] Alopecia totalis, or total loss of head hair, and alopecia universalis, or total loss of body hair, are two AA variations. Patchy AA, diffuse AA, AA reticularis, AA ophiasis, AA sisaipho, and perinevoid AA are additional clinical types. Alopecia areata's pathogenesis is poorly known. AA is thought to be a complex illness with autoimmune, hereditary, and environmental components.[5,6] According to current ideas, a dysregulated immune reaction results from the hair follicle losing immune privilege. Infected patients' growth, recurrence, or worsening of alopecia areata may be significantly influenced by viruses like SARS-CoV-2. However, the connection between COVID-19 and alopecia areata is not yet evident. This research aims to comprehensively evaluate the literature for clinical studies and accounts looking into the start of new alopecia areata or the worsening of pre-existing alopecia areata after COVID-19.[7,8] This study aims to review the existing literature systematically.

Methods

This study was a systematic review, with a systematic literature search on the PubMed, Cochrane Database of Systematic Reviews, Google Scholar, and Directory of Open Access Journals (DOAJ) databases. The search was conducted in English, using keywords related association between alopecia areata and COVID-19, including *alopecia areata, hair loss, and COVID-19*. The search was performed with a combination of some or all of these keywords, both in the title and abstract of the article. Search is limited to publications in the period February 2020 to February 2023.

Study designs included in this study were before-and-after studies with or without controls, retrospective and prospective cohort studies, interrupted time series analysis, and randomized controlled trials. Studies on interventions in both adult and pediatric patients were included if there were complete data on pediatric patients. Literature review articles, case series, letters, notes, conference abstracts, and conference articles were excluded. Data were extracted using a standardized table that includes the name of the authors, year of publication, study design, study setting, number of subjects, the treatment used, and the key findings of each study. After searching and filtering articles based on search keywords, article analysis was done manually by considering the title's and abstract's relevance. Articles that meet the inclusion and exclusion criteria that are unclear will be analyzed further by reading the full text of the article and entering the relevant information in the data extraction table. The results obtained in the included studies will be compared with those of other systematic reviews and literature.

Result

Study Selection

A systematic search was carried out and yielded 287 articles (Fig. 1). A total of 153 articles remained, after rechecking and excluding duplicated articles. A total of 27 articles were eligible for this study. Then, after a comprehensive review of the full-text articles, the remaining 6 articles were included in this study. The database search results are described in Table 1 and Figure 1. The summary of each included study is described in Table 2.

Included Articles

Of the 7 included studies, 3 were randomized case report, 2 were retrospective cohort studies, and 2 were cross-sectional studies.

Populations of Included Articles

A total of 611.380 patients were involved in the 7 included studies. The age of the research subjects varied from zero years to more than eighty years. All studies were single-center studies.

Figure 1. Systematic Search

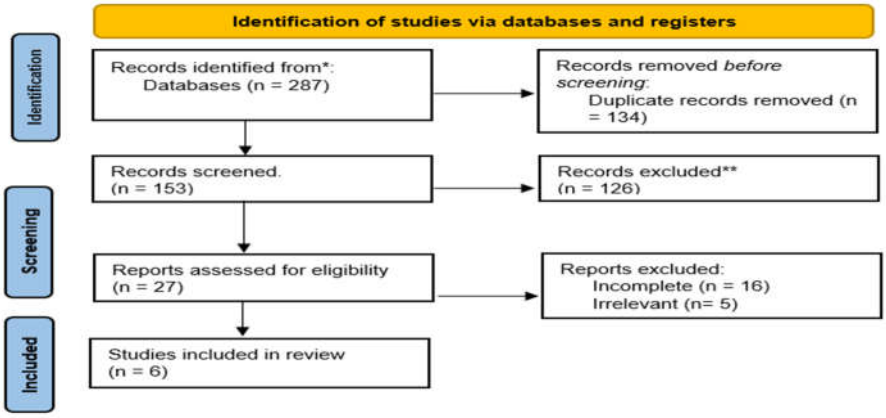

Table 1. Study Characteristics and Finding

Author	Design	Setting	Subjects	Age	Interval	Status	Clinical Findings
Phonget al, 2022[9]	Case Report	Single centre	Female (n=1)	28	1 month	New onset	Decrease in the number of anagen follicles and an increase in the number of catagen and telogenones. Surrounding inferior portions of numerous follicles show edaggregates of lymphoid cells.
Mukherjee et al, 2022[8]	Retrospective cohort	Single centre	Female (n=367.837)Male(n=2188)	0-80+	-	New onset and preexisting	Alopeciaareatawassignificantlyassociate dwithcomeincomecategories
Alkeraye et al, 2022[10]	Cross-sectional	Single centre	Female (n=490) Male (n=316)	15 - >46	1 week – more than 6 months	Newonset (n=698)	425 (52.7%) individuals had hair loss followingCOVID-19 infection, 243 (30. 1%) did not, and 138 (17.1%) were unsure if they had.
Hayrant al, 2021[11]	Case report	Single centre	Male (n=2)	10ad 13	4 weeks	New onset	A solitary 1-cm alopecic spot
Rinaldi et al, 2021[12]	Cross-sectional	Single centre	Female (n=39) Male (n=353)	27-61	2 months	New onset and pre-existed	42.5% of the subjects who also reportedhavingCOVID19infectionreporte dhavinganAArecurrence.Abouttwomont hslater,theecurrenceoftheCOVID19infect ionwasrevealed(medianof2.14month.
Kim et al, 2021[13]	Retrospective cohort	Single centre	Female (n=4.834) Male (n=3.236)	0-80+	-	New onset	In COVID-19 group, the ratio of recentlyidentifiedAAwas18/7,958(0.2%), whileincontrolswas195/218,779(0.1%).A t59.9and52.3%, respectively, there were more women than males.
Sgubbi et al, 2020[14]	Case report	Single centre	Female	54	8 weeks		Alopecia multiplex with a rapid start on the scalp'stemporoparietal region

Discussion

Alopecia areata (AA) is an autoimmune condition that destroys hair cells and causes baldness. There are many different trends and degrees of seriousness for hair loss.[4,7] AA is thought to be a complex illness with autoimmune, hereditary, and environmental components. Human Leukocyte Antigen (HLA) class II loci, UL16-binding proteins 3/6 loci, cytotoxic T lymphocyte-associated protein 5 (CTLA-4), IL-2/IL-21 locus, IL-2RA locus, and Eos locus are just a few of the immune-related GWAS findings that have been discovered in AA. These genes are involved in T cell activation and/or survival, which could increase the chance that autoreactive cells will bypass peripheral tolerance mechanisms.[15]

The anagen (active growth) phase, catagen (controlled death of epithelium cells), and telogen (resting) phases make up the normal hair development cycle. The microenvironment known as the hair follicle immune privilege, which shields a structure or organ from inflammatory responses, is preserved during the anagen phase but disappears during the telogen and catagen phases.[16,17] Inflammation causes the dystrophic anagen phase and early entry into the telogen phase in AA. Increased apoptosis during the catagen period is suggested by higher leukocyte abundance. Inflammation causes hair loss that is typically reversible because it leaves the stem cell portion of the hair shaft.[15] According to Alkeraye et al, hair loss is a dreadful side effect of COVID-19. Increases in proinflammatory cytokines (tumor necrosis factor-, interleukin 1b, interleukin 6, and kinds 1 and 2 interferons) after infection with this virus are thought to contribute to the loss of hair by harming the hair follicle progenitor cell.[10] COVID-19 as well as other virus illnesses, can result in a large release of proinflammatory cytokines, such as interleukin 6, a T-helper promoting cytokine that is important in COVID-19 and the hair follicle cycle.[9,13] However, the precise processes of hair shedding after COVID-19 infection are not well understood, and more research is needed to clarify the mechanisms.[18]

Alopecia areata deterioration is complex. Bodily strain on the body brought on by an illness, like SARS-CoV-2, may play a significant role in a patient's decline.[19] Similar to this, a pandemic or other significant life stressor may have a significant psychological impact that is a major contributor to the underlying disease's exacerbation.[10,14] This represents a significant gap in the literature examined in this review and in subsequent studies looking into the connection between alopecia areata and COVID-19. Although challenging, dissecting these fundamental causes is essential to comprehend this connection. Alkeranye et al, also found that COVID-19 patients' subjective reports of hair loss were strongly related to high body temperatures, being female, and having a history of hair loss.[8,10] Most interviewees stated that their quality of life was unaffected by hair loss following COVID-19, even though hair loss can significantly impact self-esteem and quality of life.

A former study in Italy found that 42.5% of AA patients experienced hair loss again after COVID-19. About two months after COVID-19, there was an AA recurrence. Additionally, 1-2 months after COVID-19, new-onset AA happened.[12] According to research in this study, the onset of AA generally begins around the 4th week to 2nd month. However, the onset in each person can differ as in the Alkera et al study, which reached more than six months.[8,9,11,14] The following pathways could connect COVID-19 to AA which COVID-19-induced cytokine shift, antigen mimicry between the virus and hair follicles, and COVID-19-induced tissue destruction that revealed autoantigens. The COVID-19 pandemic's psychic duress may have an exaggerated effect on AA.[20]

According to a South Korean-based study by Kim et al, there is no conclusive evidence linking a COVID-19 diagnostic to the start of new cases of alcoholism. This discrepancy may have been caused by the study design, as Kim et al study subject was nationally representative, in contrast to earlier studies that relied on small samples and could not conduct adequate statistical analysis. Kim et al, also included a sufficient control group to ensure internal validity. Given the frequency of racial differences in AA, the variation in race makeup in research could lead to inconsistency.[13]

However, it is difficult to draw any inferences due to the heterogeneity of study designs and the significant number of case reports, and more investigation is required to clarify the connection between the clinical course of alopecia areata and COVID-19.

Conclusion

COVID-19 is a disease that has very wide clinical manifestations. Cases regarding the appearance of manifestations of COVID-19 on hair have been widespread. The development of alopecia areata is generally around 4 weeks to 2 months. The exact pathomechanism of the association between COVID-19 and alopecia areata is unclear but is known to be related to inflammatory factors. However, several factors can also have an effect, such as race, age, and gender. More study is needed to clearly determine the relationship between COVID-19 and the development or exacerbation of alopecia areata.

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