## INPLASY PROTOCOL

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# Relationship between alopecia areata and intestinal dysbiosis: a scoping review protocol

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Review question / Objective: The aim of this scoping review is to determine the relationship between alopecia areata and intestinal dysbiosis to better inform clinical practice. To this end, the proposed scoping review will address the following question: What does the evidence available between 2000 and 2022 say about the possible relationship between intestinal dysbiosis and the development of alopecia areata?

Eligibility criteria: As inclusion criteria, the studies that meet the following criteria will be included for the review: studies published in any language, as long as they are translated into English or Spanish; studies published between the years 2000 and 2022; human or animal studies, considering that the human studies should be on susceptible patients with previous diagnosis of alopecia areata; studies connecting alopecia areata to the "gut-skin axis;" studies focused on therapeutic options; and finally, studies that discuss the relationship with mental health. For exclusion criteria, previous literature reviews, indexed articles that are not peer reviewed and studies that discuss additional contributing factors to the pathophysiology of alopecia areata such as genetic factors or drug-induced alopecia areata, will not be included.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 May 2022 and was last updated on 01 May 2022 (registration number INPLASY202250003).

### **INTRODUCTION**

Review question / Objective: The aim of this scoping review is to determine the relationship between alopecia areata and intestinal dysbiosis to better inform clinical practice. To this end, the proposed scoping review will address the following question: What does the evidence available between 2000 and 2022 say about the possible relationship between intestinal dysbiosis and the development of alopecia areata?

Background: Alopecia areata is an immune-mediated hair loss disorder characterized by the appearance of ovalshaped bald patches. It is the second most common type of non-scarring alopecia, with a worldwide incidence of 2%. Currently, there is no curative treatment approved by the FDA (Food and Drug Administration). There are several therapeutic options for the management of alopecia areata, however, the long-term efficacy of these treatments is minimal and the therapeutic response varies widely from patient to patient. The lack of effective therapies for the management of alopecia areata results in a problem for the quality of life of these young patients because alopecia areata has a negative effect on self-image and can lead to the development of other life-threatening diseases such as anxiety and depression.

Rationale: Gut dysbiosis is associated with an altered immune response. Considering that alopecia areata is an immunemediated disease, it is likely that gut dysbiosis may contribute to the exacerbation of alopecia areata in susceptible patients. Despite the growing interest in this line of research on possible contributing factors to the pathophysiology of alopecia areata, the evidence is still limited, which highlights the importance of further studies to expand knowledge on the subject and contribute to the development of other therapeutic alternatives that may be beneficial and effective for patients.

#### **METHODS**

Strategy of data synthesis: The search strategy will aim to locate indexed and non-indexed studies. Considering the available literature for the topics under discussion, "gray" literature, also called non-conventional literature, will be included in order to broaden the search results. The databases to be searched include PUBMED, MEDLINE, COCHRANE LIBRARY and SCOPUS. The source of studies to be used for the gray literature search to be used is Google Scholar. The keywords and MeSH terms used were: alopecia, alopecia areata, hair loss, mental

health, therapeutics, depression, anxiety, Microbiome, Microbiota, gut dysbiosis, dysbiosis.

Eligibility criteria: As inclusion criteria, the studies that meet the following criteria will be included for the review: studies published in any language, as long as they are translated into English or Spanish; studies published between the years 2000 and 2022: human or animal studies. considering that the human studies should be on susceptible patients with previous diagnosis of alopecia areata; studies connecting alopecia areata to the "gut-skin axis:" studies focused on therapeutic options; and finally, studies that discuss the relationship with mental health. For exclusion criteria, previous literature reviews, indexed articles that are not peer reviewed and studies that discuss additional contributing factors to the pathophysiology of alopecia areata such as genetic factors or drug-induced alopecia areata, will not be included.

Source of evidence screening and selection: After the search, all identified citations will be grouped and loaded into EndNote 20 using the updated 2021 version for the elimination of duplicates. After a pilot test, two independent reviewers will review the titles and abstracts to evaluate them against the inclusion criteria determined for the article. Relevant sources along with their references will be imported into the JBI Unified Information Management, Evaluation and Review System. The full text of the selected citations will be evaluated in detail against the inclusion criteria by two independent reviewers. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved with an additional reviewer. The results of the search and study inclusion process will be reported in the scoping review and presented in a flow chart based on the methodological framework of the 'Preferred Reporting Items for Systematic Reviews and Meta-analyses for scoping reviews'.

Data management: Two independent reviewers will extract data from the previously selected articles and organize the information in excel in tables with preestablished categories. In the first table the following data will be extracted from the articles: year of publication, authors, objectives of the study, methodology, results, key findings related to the research question of the scoping review. In the second table, focused on the specific objectives, the following data will be extracted from the articles: definition of alopecia areata, mechanism of pathogenesis of alopecia areata, impact on mental health, therapeutic options used and their efficacy, relationship with the intestinal microbiota.

Language: Studies in English and Spanish will be considered for inclusion.

Countries involved: Colombia.

Keywords: Alopecia areata, hair loss, microbiome, dysbiosis, gut dysbiosis, mental health.

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