

# Advancements and challenges in Hashimoto's thyroiditis research: a bibliometric analysis

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# ABSTRACT

**Aims:** Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disorder and a leading cause of hypothyroidism worldwide. This bibliometric analysis aims to provide a comprehensive overview of HT research trends, key contributors, and emerging themes by evaluating 1.309 articles published between 2004 and 2023. The study seeks to identify gaps, highlight advancements, and offer insights to guide future research efforts.

**Methods:** Data were collected from the Web of Science Core Collection database using the keyword "Hashimoto" and filtered by the "endocrinology metabolism" category. Bibliometric analysis was conducted using VOSviewer to visualize publication trends, keyword relationships, and collaboration networks. Citation metrics and publication outputs were analyzed to identify influential contributors and emerging research themes.

**Results:** The analysis revealed a steady growth in publications, peaking in 2021, with notable contributions from leading institutions and journals such as thyroid and Journal of Clinical Endocrinology & Metabolism. Dominant themes included autoimmune mechanisms, thyroid dysfunction, and the gut-thyroid axis. Emerging areas, such as microbiota-targeted interventions and personalized medicine, offer promising avenues for advancing HT research. However, regional disparities and conflicting findings in treatment strategies, including dietary interventions and supplementation, underscore the need for more robust studies.

**Conclusion:** HT research has achieved significant progress in understanding its pathogenesis and clinical management. Future efforts should focus on multidisciplinary, large-scale studies that integrate advanced technologies and address regional research gaps. By fostering global collaborations and embracing innovative approaches, the scientific community can improve patient outcomes and advance the field of HT research.

Keywords: Hashimoto's thyroiditis, autoimmune thyroid disease, bibliometric analysis, thyroid dysfunction

# **INTRODUCTION**

Hashimoto's thyroiditis (HT), known as chronic lymphocytic thyroiditis in some circles, is an autoimmune condition that results in hypothyroidism as a result of the bombarding of lymphocytic infiltration followed by the damage of the normal functioning thyroid capsules. The HT was first described by Dr. Hakaru Hashimoto in 1912 and it was this disease which brought a revolution in the field of autoimmune endocrinology.<sup>1</sup> With the passage of time, some advancement in the understanding of histology and immunology have made its characteristics well defined, for example, thyroidspecific antibodies such as thyroglobulin antibodies (TgAb) and thyroid peroxidase antibodies (TPOAb) became the signature biomarkers of the disease.<sup>2</sup> However more than a hundred years of investigation did not obtain its cause which seems even more complex because of genetic, environmental and immune factors prevailing together.<sup>3</sup>

HT is the most prevalent autoimmune thyroid disease across the globe, with internal thyroid deficiency being its main downstream effect, hypoparathyroidism. Its occurrence shows a striking prevalence among women with the female to male ratio of nearly four to one but spreads the most between the ages of 30-50.4,5 Furthermore, widespread areas with socio-economic disparities and increased age have a higher chance of occurrence, especially in areas where iodine intake is satisfactory.<sup>6</sup> HT is habitually present in combination with other autoimmune disorders such as type 1 diabetes mellitus, systemic lupus erythrematosus and rheumatoid arthritis and they are parts of autoimmune polyglandular syndromes.<sup>7</sup> This interconnectedness of autoimmune disorders raises more biomedic research questions in the domain of genetics and immunology of the patients with multiple autoimmune diseases.

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HT is known to be the most prevalent autoimmune disease and one of the contributors of endocrine disorders across the world. However, the range and breadth of scholarship on HT do not allow for the complete resolution of doubts concerning its etiology, diagnosis and therapy. The results obtained are intended to illuminate future HT research by diagnosing the main issues concerning HT, analysing areas of interest and focus, and knowledge maps construction. The significance of the problem is determined by the possibility of expanding the knowledge of the impact of HT on the public health and elaborating more efficient approaches to the management of this condition. The results of the analysis should also help in the identification of research gaps and areas of emphasis.

In this context, it is sought to contribute useful information towards the scientific progression of HT studies and to motivate interdisciplinary point of view.

# **METHODS**

Since this research is a bibliometric study, it did not require ethics committee approval. It is conducted with the institution's permission.

Data for this bibliographic analysis were obtained from the Web of Science (WoS) Core Collection platform, an authoritative resource containing high-quality, peer-reviewed scientific articles from various regions. The study focused on publications on HT and examined studies conducted between January 1, 2004 and December 31, 2023. The search was conducted using the keyword "Hashimoto" and applying the "topic" filter. Articles were selected from those included in the "endocrinology metabolism" category within WoS Categories.

As a result of the initial search, 1.678 articles were identified as focusing on HT. The titles, abstracts, and keywords of the articles were examined in detail; duplicate records were removed. Peer-reviewed articles that met the inclusion criteria were analyzed and 1.309 scientific articles were included in the final data set. The first 10 articles were independently evaluated by two researchers, and disagreements regarding selection were resolved through discussion.

Data collection was conducted between January and March 2023. The following information was collected for each article: article title, author names, publication year, journal name, journal impact factor, citation counts, country of affiliation of authors, institution name, and frequently used phrases. The obtained data were verified by two independent observers, and differences were resolved through consensus.

Bibliographic analysis was performed using VOSviewer (version 1.6.11, Leiden University, The Netherlands) to visualize research trends, keyword relationships, and collaboration networks. The main areas of focus of the analysis are:

- Annual publication trends
- Journal-specific publication trends
- Citation analysis (authors, titles, journals, and publication years)
- Keyword concurrency analysis

- Institutional affiliations and inter-institutional collaborations
- Country-level collaboration networks
- Author collaboration networks

#### **Statistical Analysis**

Descriptive statistics SPSS-(frequencies and percentages) were used to summarize publication numbers, citation distributions, and journal impact measures. Changes in annual article numbers were examined to assess temporal trends in publication output. Concurrency networks of the 150 most frequently used keywords were created to reveal thematic clusters and connections in the field.

Inter-institutional and international collaboration patterns were visualized using bibliometric mapping techniques. The density of collaborations was represented by the thickness of the connection lines, revealing common research focuses across institutions and countries. Cluster coefficients and connection densities were used to measure the integrity and integration of research themes.

# RESULTS

#### Analysis of the Distribution of Articles by Year

**Figure 1** illustrates the distribution of articles on the topic of "Hashimoto" over the years, based on Web of Science data.



Figure 1. Yearly distribution of articles on "Hashimoto"

**Figure 1** shows the year-by-year distribution of articles related to "Hashimoto." According to the data, only 33 articles were published in 2004, and this number shows a steady upward trend over the years. By 2010, the number of articles reached 57, indicating a moderate increase in interest during that period. From 2015 onward, the number of articles surpassing 96 demonstrates a growing scientific focus on the topic and increased research activity.

The year 2021 represents the peak, with approximately 98 articles published, highlighting the intense attention the topic received in scientific literature during that time. However, in the following years, a slight decline was observed, with 85 articles in 2022 and 82 in 2023. These fluctuations may reflect shifts in scientific interest or changes in research priorities during those years.

#### Journals Publishing the Most Articles on the Topic

The number of articles on the topic of "Hashimoto" published in journals within the Web of Science database is presented in Table 1.

	<b>1.</b> Journal names, number of putions of articles	publications, and	percentage
No	Name of journal	Number of article	%
1	Thyroid	133	10.16%
2	Journal of Clinical Endocrinology Metabolism	95	7.25%
3	Frontiers in Endocrinology	87	6.64%
4	Endocrine	66	5.04%
5	Endocrine Journal	60	4.58%
6	Journal of Endocrinological Investigation	58	4.43%
7	Clinical Endocrinology	53	4.04%
8	Journal of Pediatric Endocrinology Metabolism	45	3.43%
9	European Journal of Endocrinology	37	2.82%
10	BMC Endocrine Disorders	32	2.44%
11	Other	643	49.17

**Table 1** compiles data on the journals that have published the highest number of articles on "Hashimoto" in the Web of Science database. According to the data, 10.16% of the total articles (133 articles) were published in the Journal Thyroid, making it the most preferred platform for research in this field. It is followed by the Journal of Clinical Endocrinology & Metabolism with 7.25% (95 articles) and frontiers in endocrinology with 6.64% (87 articles). These journals represent key contributors to the scientific literature on the topic.

Journals with a relatively smaller share, such as endocrine (5.04%, 66 articles), Endocrine Journal (4.58%, 60 articles), and Journal of Endocrinological Investigation (4.43%, 58 articles), have also made notable contributions to the field. At the lower end of the list, BMC Endocrine Disorders accounts for 2.44% (32 articles), completing the table.

The "Other" category, which includes multiple journals not individually listed, accounts for 49.17% of the total articles (643 articles). This significant proportion indicates that research on "Hashimoto" is disseminated across a wide range of journals, highlighting the topic's broad scientific reach.

# Information on Authors, Articles, Journals, Publication Dates, and Citation Counts of the Most-Cited Publications

The authors, article titles, journals, publication dates, and citation counts of the most-cited publications on the topic of "Hashimoto" within the Web of Science database are presented in Table 2.

**Table 2** includes the authors, article titles, publishing journals, publication years, and citation counts of the most-cited publications on "Hashimoto." According to the data, the most-cited article was authored by Laurberg et al., published in 2010 in the journal Best Practice & Research Clinical

Endocrinology & Metabolism, and received a total of 335 citations. This study examines the effects of iodine intake on thyroid diseases and serves as a significant reference point in the literature.

The second most-cited article, authored by Wartofsky and Dickey, was published in 2005 in the journal Journal of Clinical Endocrinology & Metabolism and received 299 citations. This article provides evidence for narrowing the thyrotropin reference range. The third-ranked article, authored by Lee et al., was published in 2013 in European Journal of Endocrinology and received 232 citations. This study investigates the relationship between papillary thyroid carcinoma and HT using meta-analysis.

Other articles listed in the table also address various topics, such as the pathogenesis, inflammatory processes, and immune response in HT, making significant contributions to the scientific literature. For example, a study by Figueroa-Vega et al., published in 2010, examines the increase in circulating pro-inflammatory cytokines and Th17 lymphocytes in HT and has received 193 citations.

# **Publication Statistics of the Most-Cited Institutions**

The institutions affiliated with the authors of articles on "Hashimoto," the number of publications produced by these institutions, and the citation counts of these publications are presented in Table 3.

**Table 3** highlights the most-cited institutions in the Web of Science database on the topic of "Hashimoto," along with their publication counts and total citation numbers. According to the data, the most-cited institution is the University of Messina, which has produced 46 publications and received a total of 1.237 citations, demonstrating its significant influence in this field. It is followed by the University of Pisa, which has published 33 articles with a total of 1,214 citations. These two institutions have made substantial contributions to the literature on "Hashimoto" with their high citation counts.

In third place, Johannes Gutenberg University Mainz has garnered 666 citations from 14 publications, while University of Naples Federico II ranks fourth with 21 publications receiving 575 citations, and University of Turin is fifth with 18 publications earning 573 citations. The citation impact per publication of these institutions underscores their significant influence in the field.

Other noteworthy institutions include:

- Osaka University (20 publications, 551 citations),
- Sapienza University of Rome (13 publications, 481 citations),
- Sungkyunkwan University (7 publications, 471 citations).

Additionally, Odense University Hospital has achieved 467 citations from 14 publications, while the University of Birmingham, with just 5 publications, has received 452 citations, showcasing remarkable academic impact.

#### Trends in Keyword Usage

Keywords act as a bridge between the article and the targeted audience in order to increase the impact of the study.

Table 2. Most cited publications: authors, journals, publication dates, and citation counts								
Authors	Journals	Publication names	Dates	Citation				
Laurberg P, et al.	Iodine intake as a determinant of thyroid disorders in populations	Best Practice & Research Clinical Endocrinology & Metabolism	2010	335				
Wartofsky L and Dickey RA.	The evidence for a narrower thyrotropin reference range is compelling	Journal of Clinical Endocrinology & Metabolism	2005	299				
Lee J. H. et al.	The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysis	European Journal of Endocrinology	2013	232				
Figueroa-Vega N, et al.	Increased circulating pro-inflammatory cytokines and Th17 lymphocytes in Hashimoto's thyroiditis	Journal of Clinical Endocrinology & Metabolism	2010	193				
Nanba T.	Increases of the Th1/Th2 cell ratio in severe Hashimoto's disease and in the proportion of Th17 cells in intractable graves' disease	Thyroid	2009	172				
Ajjan RA and Weetman AP.	The pathogenesis of Hashimoto's thyroiditis: further developments in our understanding	Hormone and Metabolic Research	2015	167				
Zhu CL, et al.	Increased frequency of follicular helper T cells in patients with autoimmune thyroid disease	Journal of Clinical Endocrinology & Metabolism	2012	164				
Manji N, et al	Influences of age, gender, smoking, and family history on autoimmune thyroid disease phenotype	Journal of Clinical Endocrinology & Metabolism	2006	164				
Köhrle J and Gärtner R.	Selenium and hyroid	Best Practice & Research Clinical Endocrinology & Metabolism	2009	161				
Brix TH, et al	High frequency of skewed X-chromosome inactivation in females with autoimmune thyroid disease: a possible explanation for the female predisposition to thyroid autoimmunity	Journal of Clinical Endocrinology & Metabolism	2005	155				
	AuthorsLaurberg P, et al.Wartofsky L and Dickey RA.Lee J. H. et al.Figueroa-Vega N, et al.Nanba T.Ajjan RA and Weetman AP.Zhu CL, et al.Manji N, et alKöhrle J and Gärtner R.	AuthorsJournalsLaurberg P, et al.Iodine intake as a determinant of thyroid disorders in populationsWartofsky L and Dickey RA.The evidence for a narrower thyrotropin reference range is compellingLee J. H. et al.The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysisFigueroa-Vega N, et al.Increased circulating pro-inflammatory cytokines and Th17 lymphocytes in Hashimoto's thyroiditisNanba T.Increases of the Th1/Th2 cell ratio in severe Hashimoto's disease and in the proportion of Th17 cells in intractable graves' diseaseAjjan RA and Weetman AP.The pathogenesis of Hashimoto's thyroiditis: further developments in our understandingManji N, et al.Influences of age, gender, smoking, and family history on autoimmune thyroid disease phenotypeKöhrle J and Gärtner R.Selenium and hyroidBrix TH, et alHigh frequency of skewed X-chromosome inactivation in females with autoimmune thyroid disease: a possible explanation for the female predisposition to thyroid	AuthorsJournalsPublication namesLaurberg P, et al.Iodine intake as a determinant of thyroid disorders in populationsBest Practice & Research Clinical Endocrinology & MetabolismWartofsky L and Dickey RA.The evidence for a narrower thyrotropin reference range is compellingJournal of Clinical Endocrinology & MetabolismLee J. H. et al.The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysisEuropean Journal of EndocrinologyFigueroa-Vega N, et al.Increased circulating pro-inflammatory cytokines and Th17 	AuthorsJournalsPublication namesDatesLaurberg P, et al.Iodine intake as a determinant of thyroid disorders in populationsBest Practice & Research Clinical Endocrinology & Metabolism2010Wartofsky L and Dickey RA.The evidence for a narrower thyrotropin reference range is compellingJournal of Clinical Endocrinology & Metabolism2005Lee J. H. et al.The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysisEuropean Journal of Endocrinology & Metabolism2010Figueroa-Vega N, et al.Increased circulating pro-inflammatory cytokines and Th17 lymphocytes in Hashimoto's thyroiditis: further disease and in the proportion of Th17 cells in intractable graves' diseaseThyroid2019Ajjan RA and Weetman AP.The pathogenesis of Hashimoto's thyroiditis: further with autoimmune thyroid disease phenotypeJournal of Clinical Endocrinology & Metabolism2012Manji N, et alIncreased frequency of follicular helper T cells in patients with autoimmune thyroid disease phenotypeJournal of Clinical Endocrinology & Metabolism2010Köhrle J and Gärtner R.Selenium and hyroidSelenium and family history on in females with autoimmune thyroid disease: a possible endocrinology & Metabolism2006Brix TH, et alHigh frequency of skewed X-chromosome inactivation in females with autoimmune thyroid disease: a possible explanation for the female predisposition to thyroidJournal of Clinical Endocrinology & Metabolism2006				

Table 3. Most cited institutions and publication distributions according to Web of science data

No	Institution name	Number of publications	Number of citations
1	University of Messina	46	1237
2	University of Pisa	33	1214
3	Johannes Gutenberg University Mainz	14	666
4	University of Naples Federico II	21	575
5	University of Turin	18	573
6	Osaka University	20	551
7	Sapienza University of Rome	13	481
8	Sungkyunkwan University	7	471
9	Odense University Hospital	14	467
10	University of Birmingham	5	452

In this case, a list of 13 keywords most frequently used with "Hashimoto" in the WOS was included, and their frequencies of appearance in the database are presented in Figure 2.



Figure 2. Frequently co-used keywords and their usage frequency

Bibliometric analysis enabled by Vosviewer software was used for multi case studies with a minimum threshold of 5 occurrences to include a keyword in the bibliometric and systematic review. The analysis included all cases where a keyword was present but appeared a minimum of 5 times in the documents being studied. This method has ensured that only the commonly used and more significant terms are considered in the analysis. From 2.100 unique keywords only 125 were within this threshold and thus were incorporated in the analysis. This means that the analysis was only on these 125 keywords and their relations.

Due to the analysis, it was possible to pinpoint the most frequently cited keywords in a particular research field and their most important connections. Also, a total of 1,043 connections and 11 different clusters among the keywords were identified. All of these results illustrate in detail interconnections that exist among keywords in the area of the study. Such analysis is beneficial in providing understanding on the terminology of the field as well as outlining major ideas for subsequent research to be conducted. **Figure 2** depicts the keywords that are in high preference in the academic articles regarding "Hashimoto" with their respective statistics of use. As per the data, 'HT' is the most used keyword achieving a total of 339 mentions. This demonstrates that the Center's research is primarily "HT" and more importantly this term is well covered in the literature.

"Graves' disease" is the second most used keyword as it was mentioned 123 times meaning that Graves' disease is a subject of many studies in relation to "HT". The third keyword which is mostly used is "hypothyroidism", with 98 moments of touch, clearly relates to "HT" which explains why it is greatly emphasized in the literature.

Other keywords, which are not so common but which are also important include \"thyroid\" (69) or Hashimoto thyroiditis (83) and autoimmune thyroiditis (54). These terms suggest attention to autoimmune thyroid diseases together with other disorders of thyroid functions in the selected research area.

The data presented in the figure portray quite visibly the major trends and areas of concentration of research activities that have been covered in the literature on "Hashimoto." Additionally, the findings also highlight the tactical aspect of selection of keywords for increasing the adherence of studies and linkage within that area. These results suggest that research on "Hashimoto" has been quite broad in nature and even encompasses more related aspects with high degree of linkages.

#### Analysis of Inter-Institutional Publications

The findings from the analysis of the institutions affiliated with the authors of articles on "Hashimoto" and the collaborative relationships between these institutions are visualized in **Figure 3** below.

In the collaboration map created using Vosviewer software, the size of the circles represents either the number of publications by institutions or their central roles in the collaboration network. The colors of the circles indicate thematic or regional groupings. The lines between the circles illustrate the collaborative relationships between institutions, with the thickness of the lines reflecting the intensity of these collaborations. This visualization provides valuable insights for evaluating the influence of institutions in the research field, identifying strong relationships within the collaboration network, and recognizing potential opportunities for further collaboration.

Based on the figure, the key findings from the interinstitutional collaboration analysis related to "Hashimoto" are as follows:

- The graph highlights that University of Messina plays a central role in the collaboration network. With a total of 9 connections, it stands out as the institution with the highest number of collaborations. This demonstrates that the University of Messina has developed strong and extensive relationships with other institutions in "Hashimoto" research.
- Fudan University and Johns Hopkins University, each with 6 connections, hold significant positions in the collaboration network. These institutions contribute to the advancement of research in this field by fostering collaborations at both national and international levels.
- Osaka University and Ankara University, each with 3 connections, represent more limited collaboration networks but still maintain interactions with other institutions on the graph. Similarly, China Medical University, with the same number of connections, plays an active role, particularly in regional collaborations.

Overall, the intensity of the connections and the clustering structures in the graph indicate that certain institutions have become focal points in "Hashimoto" research, supporting the dissemination of knowledge through collaborative relationships in this field. Such analyses provide strategic guidance for more effectively directing academic efforts and identifying collaboration opportunities.

# **Author Collaboration Analysis**

The patterns of collaboration that emerged between the authors of articles on "Hashimoto" in Web of Science, have been examined and the results are presented in Figure 4.

Figure 4 deals with the author's bibliometric relationships who had contributed five or more studies in one area of



Figure 3. Bibliometric network visualization of inter-institutional collaborations



**Figure 4.** Bibliometric network map of author collaborations (The size of the circles represents the main authors, while the lines between the circles indicate collaborative relationships.)

research. Out of 6,789 authors who attempted to author the paper, just 121 authors who met the threshold were included in the analysis. Setting five or more works as a condition helps to capture those authors who are more focused on the synthesis of the literature and are productive enough. This also improves the credibility and significance of the results by considering only the active and productive authors.

Since this method centers on the minimal number of publications, it guarantees that the analysis is concentrated on significant scientific contributions and enhances the consistency of results. This technique disqualifies authors who have too few publications or whose cases were too atypical, and so it brings attention to the strongest authors and institutions which comprise the basic building blocks of the field. Therefore, the data analysis fully captures the cross-cutting patterns and research linkages in the region so that the analysis of the relationships of the key players in the focal literature can be done in detail. Such an approach increases the credibility of the outcomes of the study and provides good modeling of the basic scientific order in the field.<sup>8</sup>

The analysed data in **Figure 4** depicts that among the 121 authors, 8 unique clusters were formed. These clusters illustrate that authors with similar interests tend to form groups that work on the same ideas or concepts and use citations to establish interrelations. Each such cluster depicts coauthorship and information flow between the authors but at the same time, the cluster indicates research concentration pertaining to certain topics in the literature. Such bibliometric analyses do not only establish the leading researchers and the scientific networks established in the given field but also allow to obtain informative data about the changing picture of the discipline and its topic areas.<sup>9</sup>

The visualization in **Figure 4** illustrates the bibliometric connections and collaboration networks among authors working on "Hashimoto." In the visualization, each author is represented by a circle, the size of which reflects the author's contribution to the literature. The colors of the circles indicate the clusters to which the authors belong, signifying thematic or research-focused groups. The lines between the circles represent the strength of bibliometric connections, indicating the frequency of shared references and detailing the scientific relationships among authors.

The analysis of the graph reveals collaboration relationships and thematic clustering among authors in the field of "Hashimoto" research:

- The blue cluster, located in the lower middle part of the figure, represents the authors with the most extensive collaboration network in the literature. Notable authors in this cluster include Miyauchi Akira and Ito Mitsuru, who play a central role in the research area through international collaborations and high productivity. The density of connections indicates strong relationships between this cluster and other author groups.
- The red cluster, located in the left middle part of the graph, includes authors concentrated around a specific thematic framework. Zhang Jin-An and Ruchala Marek stand out

in this cluster, maintaining close scientific ties with other authors within the cluster. This cluster appears to represent thematic diversity within the literature.

- The green cluster, situated in the upper right corner, represents another significant thematic group in the field. Latrofa Francesco and Vitti Paolo are prominent authors in this cluster. The density of connections indicates strong relationships both within the cluster and with other groups.
- The orange cluster, located in the lower left corner, is a smaller group but exhibits strong internal connections. Watanabe Mikio and Matsuzuka F. are notable names in this cluster, which is focused on a specific sub-theme. Despite its narrow research focus, this cluster contributes meaningfully to the literature.
- The yellow cluster, concentrated in the upper middle part of the graph, highlights authors such as Trimarchi Francesco and Ruggeri Rosaria Maddalena. This cluster represents scientific interactions among authors with a thematic research focus.
- The turquoise cluster, on the right edge, includes authors like Tommaso Aversa and Andrea Corrias, who contribute to the literature through high levels of collaboration.
- The purple cluster, situated in the upper left, includes authors such as Monica Marazuela and Weiping Teng.

Overall, the density of connections and clustering structures in the graph clearly illustrate the breadth and depth of collaboration relationships in the literature. This visualization serves as a crucial tool for understanding the leading authors and thematic groups in the field.

# **Country-Based Distribution of Citations**

A comprehensive assessment was conducted based on countries on the articles that pertained to the topic of "Hashimoto" and are part of the WoS database. The results of this analysis are visualized in **Figure 5** and show a clear citation diffusion trend geographically.



Figure 5. Analysis of citation

**Figure 5** gives clear images depicting the analytical view of the mapping out of the citations distribution by country for articles in the WoS and the inter country academic collaborations. For further analysis countries which managed to publish five or more documents were included (41 out of 72 countries that met the inclusion criteria). A total of six clusters were identified in this analysis, each defined with a particular theme of research or a common network of collaboration.

The figure depicts the distribution and the geography of the citations for research work done on the topic "Hashimoto" as well as the inter- country academic collaborations. Each circle represents a country and the area of the circumference is proportional to the area of the contribution of that country in the literature. The lines between such circles are collaborative links and graphically, the thicker the line the more the covalterations occurred. The colors in the figure demonstrate the arrangements of nations in groups, and the collaboration networks that are formed around specific theme of the research work done.

As seen from the figure there is a large circle at the center depicting the United States whose contribution has been great in the literature and the countries working collaboratively with other countries networks. This central role of the U.S. demonstrates its leadership and influence in Hashimoto research in the world. Among the European countries, the more advanced ones are the United Kingdom, Germany and France. These countries are more nearer to the center circle of the figure and have closer collaborative relations with each other which means that they form a well-connected scientific network in Europe. Also, the U.K. has created strong links with the U.S. which adds to its prominence in the literature. In Asia it is the countries such as Japan, China and Korea which play a more active role. These countries are prominent from the regional and international perspectives because of their strong networks with the U.S. His figure reminds us how Japanese researchers and professionals have been positioned in the international scene in terms of the geocentric model for "Hashimoto" research. Turkey can be seen at the middle of the figure as both a European continent and an Asian country giving it a unique opportunity of being a link between the two clusters. This location helps to explain Turkey's presence in the literature as well as its potential for cross border collaborations.

Such nations depicted by smaller circles which are places on the borders of this figure are, in turn, indicated as having less of an influence on the literature. It is however important to note that these nations also participate in regional collaboration networks.

To sum up, the regional collaboration networks in the field of "Hashimoto" research are shown in **Figure 5**. The US, UK and Japan are becoming quite prominent in the field as the core countries apart from Turkey and other countries in Asia that show good potential for collaboration. Thus, this sort of visualization helps the readers understand the important contributors and engagement patterns of the countries in the collaboration within the literature.

# DISCUSSION

Taking into account the findings of this scientific study, it also becomes evident which specialized researchers and groups of researchers are actively participating in the development of the field and what directions and themes are becoming popular. However, there is no dispute that given the evidence these works bring, the field of inquiry needs a more in depth assessment at both its advances and challenges.

The trend of increasing concern in respect of scientific publications first noticed in 2004 and continuing up to the present time with the 170 articles registered in 2021 shows the growth in the interest in research into and development of auto immune thyroid diseases. This accords with the rise in prevalence of autoimmune thyroid disease and new methods of treatment which were reported by Tao et al. in 2023. That there has been a slight decrease in publications within the subject matter after 2021 could be due to change in interests or other imposing issues such as the COVID-19 pandemic. Such a situation may warrant the change of interests or the limited number of resources may constrain the effort in this particular area as Ahmed et al.<sup>2</sup> and Akamizu and Amino<sup>6</sup> have observed.

As reported by Hu et al.<sup>10</sup> there has been noticeable growth in studies about epidemiological and worldwide distribution trends, especially in parts of the world which are backwards, which denotes some improvements in diagnosis and awareness. On the other hand, Ragusa et al.<sup>11</sup> lamented that even though there are more scientists trying to research the disease, there remains high ignorance of the geographical and ethnical heterogeneity of the disease which remains a concern for this present study.

There are substantiating evidences which show Thyroid and Journal of Clinical Endocrinology & Metabolism as being key in the communication of meaningful research findings. In due course, they become influential in the study of HT. These findings also imply that research such as those by Zaletel and Gaberscek<sup>3</sup> examining the interactions of genetics and the environment are also common in these journals. However, Sawin<sup>1</sup> noted that A historical approach to the disease suggests that it is possible there was a relative famine of research on HT in some earlier periods.

The pair of studies of Wartofsky and Dickey (2005) on thyrotropin reference ranges and of Laurberg et al. (2010) on the role of iodine intake and thyroid diseases worked towards the development of some clinical guidelines. However, there are also some contradictory findings. For instance, Krysiak et al 2019 report limited effect of such nutritional interventions like gluten-free diet on the disease outcomes and challenge the wider impact of the nutritional interventions suggested by Ihnatowicz et al. (2020). Such contradictions emphasize the necessity of further randomized controlled interventions to definitively demonstrate the evidence supporting specific dietary recommendations.

The bibliometric analysis touches upon the major themes, which include "HT", "Graves' disease" and "hypothyroidism" This corresponds with the observations made by Pyzik et al.<sup>12</sup> who noticed that there is an emphasis on immune system dysfunction as a area of study. Other emerging areas such as microbiota and gut-thyroid axis are also promising. As shown by Fernandez-Garcia et al.<sup>13</sup> and Liu et al.<sup>14</sup>, it is possible to target microbiota in order to regulate thyroid autoimmunity. The term "HT" appears to be the most prominent among

key words appearing in the literature and this is similar to Radetti's<sup>4</sup> study which attempted to investigate clinical features of pediatric Hashimoto's disease. Of course, other keywords including "Graves' disease" and "hypothyroidism" are important due to the idiopathic nature of the disease with many autoimmune phenomena. Although these works postulate many positive correlations between gut health and autoimmunity, Lerner et al.<sup>15</sup> cautioned that generalizations ought to be made bearing in mind some reproduction and heterogeneity limitation in study design. Such results also indicate an unproven, and quite broad approach to the gutthyroid axis. Such well-cited studies are represented by the University of Messina and the University of Pisa. Such European institutions also to some extent contribute as seen in Ragusa et al.<sup>11</sup> in examining thyroid autoimmunity.

Also, other authors such as Miyauchi Akira, Ito Mitsuru also contributed towards the principles of HT pathogenesis at the clinical level and molecular level. These findings conform to the set up views emphasized by Ahmed et al.<sup>2</sup> and Akamizu and Amino<sup>6</sup> that knowledge transfer and collaboration enhances research output. But, the absence of such research works in developing countries, in the same way contributes to limiting the prospect of research.

But, certain areas such as Africa and South America are less noted in the body of literature. According to McLeod and Cooper<sup>16</sup> that these regions' contributions in this arena need be looked at in view of genetic and environmental influences on autoimmune thyroid diseases.

Concepts regarding the management of HT still remain a contentious domain. Research of this type e.g. Pirola et al.<sup>17</sup> confirms the opinion that subclinical hypothyroidism can be treated by selenium supplementation, on the contrary dispute on the fact that such measures will be useful in the long run.

The increasing number of studies on vitamin D and selenium suggests a growing interest in immunomodulatory approaches to managing HT. This finding supports the notion that research on HT has expanded beyond traditional endocrinological assessments to include nutrition and adjunctive therapeutic approaches as significant areas of investigation. Furthermore, Shin et al.<sup>18</sup> reported an association between low vitamin D levels and increased antithyroid peroxidase antibody titers, Nodehi et al.<sup>19</sup> found that vitamin D supplementation alone failed to significantly alter disease progression, and Pirola et al.<sup>17</sup> showed that selenium supplementation may be beneficial in some patients. Such conflicting findings highlight the need for larger, more comprehensive randomized controlled trials. This highlights the complexity of autoimmune thyroid diseases and the need for multifaceted treatment strategies.

When analyzing the available research on HT there is an ongoing theme that this is a very broad field that keeps changing with the advancements being made. There are considerable advances toward the epidemiological understanding, due care toward the pathogenesis and the disease management resulting in the paradoxes witnessed as it relates to various interventions being dietary, vitamin D, supplementation or the risk for cancer. To solve this issue, large population-based multi-centric studies should be the key focus of further research in this area. Furthermore including new platforms such as microbiota and precision medicine can further enhance the prevention and treatment strategies. This task can be achieved through increased collaboration between different scientific disciplines and tackling local issues in the research on HT which in turn would improve the research fit for translation enablers.

# Limitations

This study has some limitations. First, the analysis is restricted to the Web of Science Core Collection, excluding relevant articles from other databases. Second, it only covers publications from 2004 to 202, potentially missing earlier trends and historical perspectives. Third, using the term "Hashimoto" as a search criterion may have excluded relevant studies with different terminology. Lastly, limited research from developing countries may overlook regional differences and contributions to HT research.

# CONCLUSION

Research in this field focused on HT has shown tremendous growth in the last 20 years which has increased the understanding of its diverse pathophysiology, epidemiology and treatment aspects. The findings obtained through this bibliometric analysis stresses the increasing patterns of alliances across the globe in research initiatives targeting HT as indicated by the rising number of publications, changing trends in cross border research and increasing number of international linkages. However, the findings also point out areas still faced with challenges such as the inability to explain wide variations in contribution to research from different regions to the problem of RT, certain evidences on some therapeutic approaches being contradictory, and the more recent areas such as the gut-thyroid link and other aspects requiring more focus being barely scratched.

In order to tackle those mentioned above, longitudinal studies of a multidisciplinary and multicenter nature should be the focus of future studies, as they afford the opportunity for the employment of newer diagnostic and treatment approaches, for instance, microbiota profiling and genomic analysis. Of equal importance is promoting greater involvement of gaps in regions and populations so that the findings can be more widely applied and approaches more culturally appropriate.

By bridging knowledge gaps and embracing innovative methodologies, the scientific community can advance the understanding of HT and improve clinical outcomes for patients worldwide.

# ETHICAL DECLARATIONS

# **Ethics Committee Approval**

Since this research is a bibliometric study, it did not require ethics committee approval.

# **Informed Consent**

Since this research is a bibliometric study, it did not require informed consent.

#### **Referee Evaluation Process**

Externally peer-reviewed.

#### **Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

#### **Financial Disclosure**

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#### **Author Contributions**

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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