



CURRENT STATUS OF THALASSEMIA MINOR STUDIES

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Abstract: Thalassemia minor carriage is one of the most common causes of anemia in Mediterranean countries. This study aimed to investigate the publications in scientific journals on thalassemia minor, which is an important health problem, especially in Mediterranean countries. The goal of this study was to retrieve data from journals that were indexed in the Web of Science (WoS; Thomson Reuters, New York, NY, USA) database. The WOS Core Collection was used to retrieve comprehensive bibliometric data. Keywords related to "beta-thalassemia carrier," or "beta-thalassemia trait," thalassemia minor" or "heterozygous beta-thalassemia" were used in a search query in the WOS search engine. The time frame was specified since 10 March 2022. The analysis included information on the increase of publications, the most active countries and institutions, the most cited journals, and the mapping of publications and keywords. A total of 8618 publications were retrieved. The first article was published in 1970, and the period between 1970 and 2021 was searched. The maximum number of publications was published in the year 2021. The number of publications had increased since 2009. Most of the publications were articles (61.696 %). The publications were from more than 100 disciplines and most of them were from Hematology (49.176%). The publications were from 274 different countries. Most of the publications were from the USA, Italy, and Greece. The USA is at the top of the list in the number of publications. But with active funding and support from the governments especially the Mediterranean countries, which have a higher prevalence of thalassemia minor, the productivity of scientific research should be increased.

Keywords: Thalassemia minor, Publication, Bibliometric analyses

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1. Introduction

The term thalassemia comes from the Greek words thalassa (sea) and haima (blood) (Galanello and Origa, 2010). Anemia is a common disease that affects people all over the world. Nutritional anemia is the most common type of anemia in children. However, thalassemia minor carriage is one of the most common causes of anemia in Türkiye and Mediterranean countries (Kabasakal et al., 2018; Arslan Maden et al., 2020). Thalassemia major, thalassemia intermedia, and thalassemia minor are the three main types. Thalassemia minor is also known as "beta-thalassemia carrier," "beta-thalassemia trait," or "heterozygous beta-thalassemia." (Galanello and Origa, 2010).

Beta-thalassemia's are a set of inherited blood illnesses marked by abnormalities in the synthesis of hemoglobin's beta chains, resulting in phenotypes ranging from severe anemia to clinically asymptomatic people. The global yearly incidence of symptomatic persons is estimated to be 1 in 100,000, with 1 in 10,000 people living in the European Union (Galanello and Origa, 2010; Arslan Maden et al., 2020). Thalassemia minor has traditionally been more prevalent in specific parts of the world, such as the Mediterranean, the Middle East, and Southeast Asia (Kattamis et al., 2020).

Because of being a benign hematological disease of the thalassemia trait, diagnosis can be easily missed in hospital admissions of patients who have not been diagnosed yet. Thalassemia trait is a disease which can most often intermingle with iron deficiency. Various formulas have been developed in clinical practice to differentiate or not miss the diagnosis of thalassemia trait (Merdin, 2018).

Testing for Hb electrophoresis immediately in those with high ferritin levels and after iron treatment in those with low levels will enable early detection of thalassemia carriers and make genetic counselling possible (Oğuz et al., 2009). More than 40 mathematical indices have been proposed in the hematological literature to differentiate thalassemia trait from iron deficiency anemia. None of these discriminant indices is 100% sensitive and specific, and also the ordering of discriminant indices is not consistent. In a meta-analysis with the most used discriminant indices, it was found that the M/H (microcytic and hypochromic percent) ratio outperformed all other discriminant indices in distinguishing between iron deficiency anemia and thalassemia trait. While the sensitivity and specificity of the M/H ratio are not high enough to make a definitive diagnosis, it is certainly valuable for identifying patients with microcytic RBC for whom diagnostic testing is



indicated to confirm thalassemia (Hoffmann et al., 2015). However, discriminant indices that are superior in one study may perform worse in another study.

Additional serum iron, total iron binding capacity and ferritin levels should be checked in patients who are thought to be thalassemia trait with Mentzer Index values calculated from the MCV/RBC ratio. In addition to all these basic blood samples, laboratory tests such as hemoglobin analysis (HbA 2 and abnormal Hb) and DNA analysis are key parameters for differentiating thalassemia and iron deficiency anemia (Hoffmann et al., 2015). Newborn and prenatal screening, prenatal diagnosis and counselling are keys to early detection and prevention of thalassemia (Farzana et al., 2015).

This study aimed to investigate, identify, and characterize the publications in scientific journals on thalassemia minor, which is an important health problem, especially in Mediterranean countries.

2. Material and Methods

The goal of this study was to retrieve data from journals that were indexed in the Web of Science (WoS; Thomson Reuters, New York, NY, USA) database. The WOS Core Collection was used to retrieve comprehensive bibliometric data and the SCI-EXPANDED, SSCI, A & HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI indexes database, which has previously been regarded the optimal database for bibliometrics (Alkan et al., 2021; Alkan-Çeviker et al., 2021a; Öntürk et al., 2021; Özlü, 2022).

Keywords related to "beta-thalassemia carrier," or "beta-thalassemia trait," thalassemia minor" or "heterozygous beta-thalassemia" were used in a search query in the WOS search engine.

"United Kingdom English and United States English

words utilized" for more accurate results. The time frame was specified since 10 March 2022. The analysis included information on the increase of publications, the most active countries and institutions, the most cited journals, and the mapping of publications and keywords.

As indices of the influence of publications, the Hirsch (h) index of the publishing journal was utilized.

3. Results

In this study, a total of 8618 publications were retrieved. The first article was published in 1970, and the period between 1970 and 2021 was searched. The maximum number of publications was published in the year 2021. The number of publications had increased since 2009 (Figure 1).

Most of the publications were articles (61.696%) (Table 1). The publications were from more than 100 disciplines and most of them were from Hematology (49.176%) (Table 2). The publications were published 23.606 by different authors. Suthat Fucharoen from Mahidol University, Thailand was the most productive author on thalassemia minor study with 200 publications.

The publications were from 274 different countries. Most of the publications were from the USA, Italy and Greece. Türkiye ranked 7th (Table 3).

Most of the publications were from the National and Kapodistrian University of Athens, Greece (3.655%) (Table 4).

The United States Department of Health Human Services funded most of the studies (Table 5).

2.1. Citing Analyses

8618 publications were cited 112633 times and H index was 116. The number of citations were increased by the years (Figure 2).

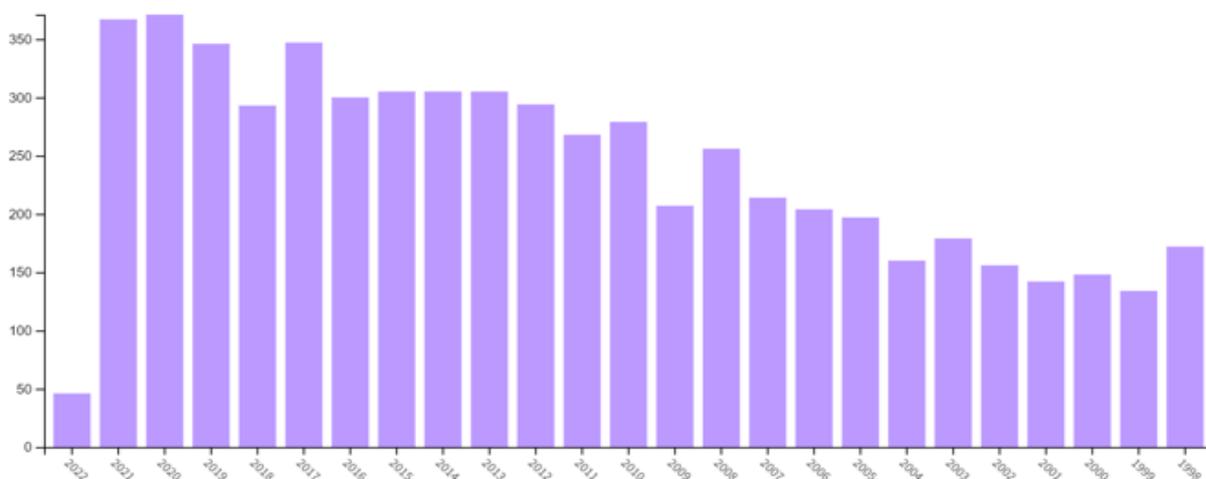


Figure 1. Number of the publications by the years (2022 did not completed yet).

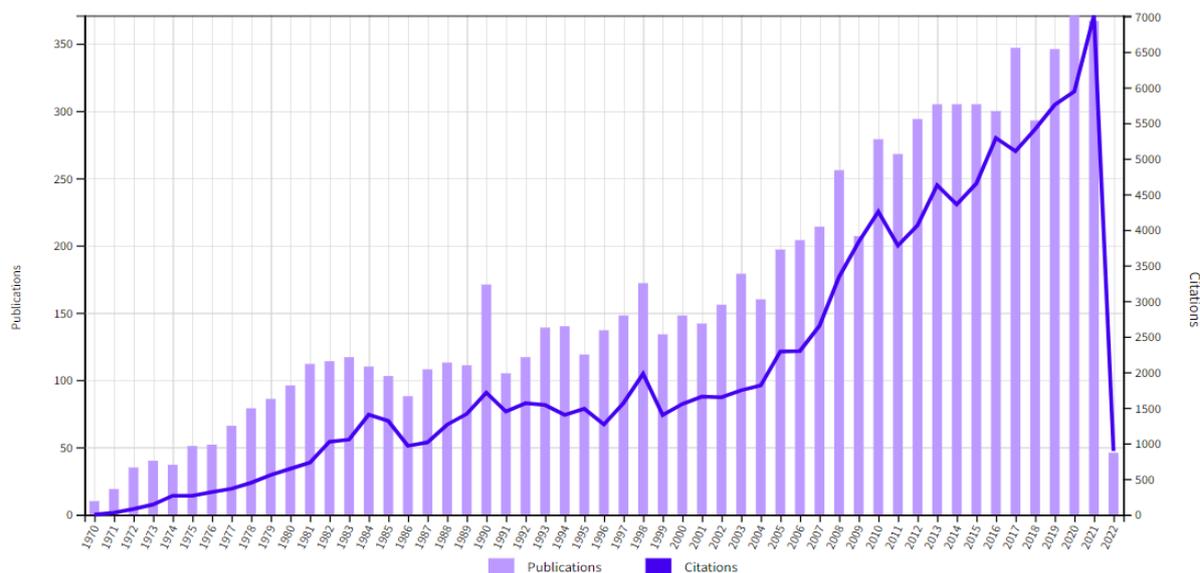


Figure 2. Number of publications and citations by the years.

Table 1. Types of the documents (n=8787)

Document Types	n	%
Articles	5317	61.696
Meeting Abstracts	1964	22.790
Letters	610	7.078
Review Articles	248	2.878
Notes	211	2.448
Proceedings Papers	171	1.984
Editorial Materials	137	1.590
Corrections	50	0.580
Early Access	41	0.476
Book Chapters	18	0.209
News Items	13	0.151
Corrections, Additions	4	0.046
Discussions	2	0.023
Data Papers	1	0.012

Table 2. Study disciplines (n=8618)

Web of Science Categories	n	%
Hematology	4238	49.176
Biochemistry Molecular Biology	994	11.534
Medicine General Internal	787	9.132
Pediatrics	766	8.888
Genetics Heredity	648	7.519
Medicine Research Experimental	516	5.987
Oncology	411	4.769
Immunology	240	2.785
Multidisciplinary Sciences	223	2.588
Obstetrics Gynecology	208	2.414

Showing 10 out of 128 entries, 7 record(s) (0.081%) do not contain data in the field being analyzed.

Table 3. Number of publications according to countries (n=8618)

Countries/Regions	n	%
USA	1734	20.121
Italy	1330	15.433
Greece	700	8.123
England	639	7.415
Iran	611	7.090
India	556	6.452
Türkiye	477	5.535
Thailand	471	5.465
Peoples Republic of China	452	5.245
France	396	4.595
Egypt	300	3.481
Israel	272	3.156
Canada	225	2.611
Pakistan	186	2.158
Australia	166	1.926
Germany	159	1.845
Lebanon	153	1.775
Switzerland	132	1.532
Saudi Arabia	122	1.416
Netherlands	118	1.369
Brazil	117	1.358
Japan	117	1.358
Spain	114	1.323

274 record(s) (3.179%) do not contain data in the field being analyzed.

Table 4. Number of publications according to affiliations (n=8618)

Affiliations	n	%
National Kapodistrian University of Athens	315	3.655
Mahidol University	304	3.528
University of London	261	3.029
Egyptian Knowledge Bank	260	3.017
Assistance Publique Hopitaux Paris	225	2.611
University of Cagliari	225	2.611
University of California System	209	2.425
University of Milan	207	2.402
University College London	197	2.286
Institute National De La Sante Et De La Recherche Medicale Inserm	192	2.228
University of Oxford	189	2.193
Augusta University	187	2.170
University System of Georgia	187	2.170
Hebrew University of Jerusalem	173	2.007
Universite de Paris	168	1.949
University of California San Francisco	168	1.949
Harvard University	165	1.915
Cornell University	152	1.764
American University of Beirut	149	1.729
Shiraz University of Medical Science	148	1.717
Consiglio Nazionale Delle Ricerche	146	1.694
University of Ferrara	144	1.671
University of Pennsylvania	136	1.578
Laiko General Hospital	135	1.566
Irccs Ca Granda Ospedale Maggiore Policlinico	131	1.520

Showing 25 out of 4904 entries, 277 record(s) (3.214%) do not contain data in the field being analyzed.

Table 5. Summary of the funding agencies (n=8618)

Funding Agencies	n	%
United States Department of Health Human Services	451	5.233
National Institutes of Health Nih USA	446	5.175
Nih National Heart Lung Blood Institute Nhlbi	303	3.516
Nih National Institute of Diabetes Digestive Kidney Diseases Niddk	156	1.810
National Natural Science Foundation of China	98	1.137
European Commission	83	0.963
Thailand Research Fund	63	0.731
Fondazione Telethon	45	0.522
Novartis	39	0.453
Shiraz University of Medical Sciences	35	0.406

Showing 10 out of 1518 entries; 6928 record(s) (80.390%) do not contain data in the field being analyzed.

4. Discussion

Bibliometric analysis is a way of quantifying scientific publications to estimate a researcher's, journals, countries, etc. research productivity. Gaps in study areas

can be found and even comparisons of prior studies on a topic (Alkan Çeviker et al., 2021b; Durgun, 2021; Dindar Demiray et al., 2021a; Dindar Demiray et al., 2021b; Gürler et al., 2021; Köylüoğlu et al., 2021; Küçük et al., 2021; Özlü, 2021a; Özlü, 2021b; Mızrakçı, 2022; Akyüz et al., 2022). In bibliometric analysis, Internet databases are commonly used. While this method was widely utilized in earlier years in social field studies, it has successfully been applied in medicine, which is our field. Visualization approaches can be used to examine and map various databases. Several descriptive statistics can be used in the bibliometric analysis, including citation data, network analysis based on citations that cover journals, authors, nations, keywords, academic and research institutions, and frequency analysis. It can also provide information on research clusters, present interests, and emerging topic trends. (Durgun, 2021; Gürler et al., 2021; Köylüoğlu et al., 2021; Küçük et al., 2021; Özlü, 2021a; Akyüz et al., 2022; Mızrakçı, 2022). Similar studies were also conducted in the field of hematology (Okoroiwu et al., 2020; Seo et al., 2020; Chen et al., 2021). There were even bibliometric analyzes on anemia (Awe et al., 2021; Frater, 2021). However, in the accessible literature, there was no similar study published on thalassemia minor. We sought to provide a bibliometric summary of the literature on thalassemia minor from 1970 to 2021 in this study. This work especially will shed light on showing researchers, the most active institutes, citations, countries, and beneficiaries.

A total of 9031 articles on thalassemia minor were published in 10 different fields in the Web of Science research field. The distribution of the top 10 research areas in thalassemia research is listed in Table 2. "Hematology" was undoubtedly the dominant research area with 4238 articles and followed by "biochemistry, molecular biology", "Internal General Medicine", "Pediatrics", "Genetic Heredity" and "Medicine Research Experimental" in Table 2. "Hematology", which made up 49.176% of the total publications, was at the top of the list. This analysis shows that research points come to the fore in basic sciences such as molecular biology, genetics, experimental medicine and clinical sciences such as hematology and pediatrics, which is related to the prevention, diagnosis and treatment of thalassemia.

It was found that the publications were from 274 different countries. Most of the publications were from the USA, as in previous bibliometric analysis on different topics (Durgun, 2021; Gürler et al., 2021; Köylüoğlu et al., 2021; Küçük et al., 2021; Akyüz et al., 2022; Mızrakçı, 2022). Also, Italy and Greece were in the top 3 countries on thalassemia minor research. Among the first 23 countries that published article rates (Table 3), the USA has the biggest share with 20.121 %. Italy follows it with 15.433% and Greece with 8.123% respectively. Türkiye ranked 7th. Most of the publications were from the National and Kapodistrian University of Athens, Greece. The fact that countries excluding the USA are at the top can be attributed to the high prevalence of this disease in

these countries. Almost all of the regions in the top 20 are countries with good economic income. Therefore, it has been suggested that they contribute more easily to valuable scientific and academic publications. It is thought that easy and better access of the patients to health centers for screening and diagnosis and the different effects of environmental genetic factors in Western countries may contribute to this situation.

Scientific efficiency is associated with research and development expenditures (Nag et al., 2013; Acosta et al., 2014, Ebadi and Schiffauerova, 2016). Table 5 lists the 10 most important institutions in this field. United States Department of Health Human Services topped the list with 451 funded articles. In the second place is the National Institutes of Health (NIH) in the USA with 446 articles. In the third and fourth places are NIH National Heart Lung Blood Institute (NHLBI) and NIH National Institute of Diabetes Digestive Kidney Diseases NIDDK, affiliated with NIH. The NIH stands out as one of the world's largest biomedical research funders and the largest funder overall. In addition to these, Novartis pharmaceutical company was included in the top 10 as one of the financing institutions, which the only for-profit pharmaceutical company. The true prevalence of thalassemia in the United States is unknown; however, it is noteworthy that with the increasing Asian immigration in America (Hoppe, 2009), more information is sought on the effect and course of hereditary disorders on diseases. Most of the funding affiliations were from the USA, and this situation may lead to the number of publications from the USA being higher than in other countries. But this topic seems to be important in Mediterranean countries, especially in Greece and Italy.

The 25 most productive institutes between 1970 and 2021 are listed in Table 4. Seven different institutions from the USA, 4 from Italy, 2 from Greece and 2 from the UK are leading the list. This distribution reiterated the numerical superiority of the United States in the field of research on thalassemia minor. The fact that institutions with high publication numbers are predominantly from the USA, Italy, Greece, and the UK indicates that these countries have outstanding academic institutions, talents and research culture in the field of thalassemia minor. One of the world's most historic, largest and oldest university centers, the National Kapodistrian University of Athens has contributed 315 more publications, than any other institution, accounting for 3.655% of the world's publications in this field. Mahidol University in Thailand was the second in efficiency with 304 publications and 3,528% of the total publications. The University of London from the UK and Egyptian Knowledge Bank ranked third and fourth, respectively.

There are certain limitations of this bibliometric analysis. First, we have only used a single medical database-WOS, for our analysis. We chose the WOS database because it offers both basic and advanced search possibilities. It is worth noting that the WOS does not index all journals. Other electronic databases, such as PubMed, Embase,

SCOPUS, Google Scholar, and the Cochrane Library, are not searched or examined. Although different databases return vastly different results (Falagas et al., 2008; Kulkarni et al., 2009) it is acceptable to use a single medical database to identify top-cited medical research articles—many published bibliometric analyses have used the SCIE database for this purpose (Oh and Galis, 2014; Azer and Azer, 2016; Zhang et al., 2016). To find all material on the issue, we searched all publications, including books, journal articles, letters, and clinical trials. We assigned articles to the country of the first author where they had writers from two or more member countries.

Non-English papers were also excluded. Most of the studies in this study are written in English; nonetheless, this limitation may result in a publishing bias. The final constraint is that influential publications were not referred to frequently enough because some potentially influential papers were released recently and could not be cited frequently. Another restriction is that the data for 2022 is incomplete due to the lack of information. And the collaboration and detailed citation analyses did not do, as it needs other programs.

It has been determined that the publication of articles published over the years is generally in an increasing trend, with a few exceptions. The reductions in the number of exceptions decreased from 1998 to 1999, from 2003 to 2004, from 2008 to 2009, and from 2017 to 2018. No significant data and events related to the causes of these decreases were found. While new developments in the treatment of thalassemia, the discovery of targeted therapy molecules, and specialized treatments such as bone marrow transplantation remain current, they may have contributed positively to the emergence of publications in this field as an author comment. However, in general, a net positive and significant relationship was not found with the increase in publications. Overall, the thalassemia minor has attracted increasing attention and has become one of the hottest research areas in hematological research.

A similar upward trend is observed in citations to publications. Specifically, the sharp upward trend in 1990 and 1998 entered a downward trend in consecutive years, 1991 and 1999. The number of citations is also increasing, except for the isolated periods, which have a ripple effect in this generally increasing trend.

The number of publications and citations has increased over the years. This could be due to an increase in global publications on all topics. And also, Patients' access to diagnostic solutions may be easier, health care services may be increased, and genetic screenings and family screenings may be more frequent. For this reason, it became easier to carry out the study by reaching more patient numbers.

5. Conclusion

The USA is at the top of the list in the number of publications. But with active funding and support from

the governments especially the Mediterranean countries, which have a higher prevalence of thalassemia minor, the productivity of scientific research should be increased.

Author Contributions

Concept: G.C. (50%) and C.Ö. (50%), Design: G.C. (50%) and C.Ö. (50%), Supervision: G.C. (100%), Data collection and/or processing: G.C. (50%) and C.Ö. (50%), Data analysis and/or interpretation: G.C. (50%) and C.Ö. (50%), Literature search: G.C. (50%) and C.Ö. (50%), Writing: G.C. (50%) and C.Ö. (50%), Critical review: G.C. (50%) and C.Ö. (50%), Submission and revision G.C. (50%) and C.Ö. (50%). All authors reviewed and approved final version of the manuscript.

Conflict of Interest

The authors declared that there is no conflict of interest.

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Ethical Approval/Informed Consent

The study complied with the Helsinki Declaration, which was revised in 2013. Ethics committee approval is not required as there is no human or animal research.

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