



Scientific Research on the Pineal Gland: A Bibliometric Analysis from Its First Publication

ORIGINAL ARTICLE Endocrinol Res Pract. 2024;28(2):65-70

ABSTRACT

Objective: The bibliometric perspective examines publications using a quantitative way and statistics to analyze them. The purpose of the current study was to perform a comprehensive overview of the research on the pineal gland through bibliometric methods to determine the trends and rare topics related to the gland.

Methods: The Web of Science database was used to identify the publications associated with the gland. The literature review exposed a total of 8719 publications. The identified publications were analyzed using the bibliometric approaches (VOSviewer Version 1.6.13).

Results: The first studies on the pineal gland were in the 1970s. The most prolific country is the United States (2451). It was seen that most of the articles were published in Journal of Pineal Research. The majority of publications (97.09%) were written in English. The most prolific author is Reiter, Russel J. Moreover, the most prolific institute is the Centre National De La Recherche Scientifique (France). The most popular keywords in the articles were pineal gland, melatonin, circadian rhythm, rat, retina, photoperiod, circadian, aging, serotonin, oxidative stress, and brain.

Conclusion: The results indicated the researchers' interest in the gland and provided quantitative data about the place of the gland in the scientific area. Studies on this subject have tended to increase in recent years. As far as we know, this research is the first bibliometric study to provide a comprehensive analysis of scientific publications with an emphasis on the pineal gland since 1976.

Keywords: Pineal gland, epiphysis cerebri, conarium, pineal body, VOSviewer

Introduction

The pineal gland (PG, synonyms are pineal body, conarium, and epiphysis cerebri), which is also known as a "mystery or mystic gland", is the least understood endocrine gland and was the last part of the endocrine system to be discovered. 1,2 Apart from the "third eye," the PG has also been described as "the seat of the soul," "the part of the body in which the soul directly exercises its functions," "the intuition organ," "the connection structure between body and spirit," and "the center at which the soul and body interact."3 The gland is situated in the epithalamus, between the 2 cerebral hemispheres, in a groove where the two halves of the thalamus join. Also, it contacts directly with the 2 recesses of the 3rd ventricle, the pineal recess and the dorsal supraspinal recess, which includes the choroid plexus. Moreover, it is located in the posterior part of the 3rd ventricle, between the posterior commissure and the dorsal habenular commissure.4 The location of the PG, along with its unique characteristics and morphological appearance, has awakened the interest of many researchers and scientists.⁵ It has been observed that the gland has been the subject of valuable research over both past and recent years. Bibliometric analysis provides an objective way for an effective and detailed evaluation of the past, current, and future states of many scientific publications in a specific field.⁶ This analysis method includes features such as the document type, content of the article, number of citations to the article, number of interested authors, the affiliation of authors, index, and category of the journals. In this way, bibliometric studies allow us to identify the global research, dynamics, and trends in a scientific topic during a period.8 From this perspective, we aimed to conduct an extensive and holistic bibliometric analysis of the publications related to the pineal gland to determine the research trends and identify rarely studied topics on the gland.

Materials and Methods

Articles related to the pineal gland were accessed through the Web of Science (WoS) database by the Thomson Reuters Institute for Scientific Information, using the keywords "pineal



Copyright @ Author(s) – Available online at http://endocrinolrespract.org This journal is licensed under a Creative Commons (CC BY-NC-SA) 4.0 International License. Esra Şen¹ Sinem Nur Sever²

Begümhan Turhan¹

¹Department of Anatomy, Başkent University Faculty of Medicine, Ankara, Turkey ²Department of Anatomy, Atılım University Faculty of Medicine, Ankara, Turkey

Corresponding author: Begümhan Turhan ⊠ begumhanturhan@baskent.edu.tr

Received: December 26, 2023 Revision Requested: February 9, 2024 Last Revision Received: February 10, 2024 Accepted: March 3, 2024 Publication Date: April 1, 2024

Cite this article as: Şen E, Sever SN, Turhan B. Scientific research on the pineal gland: A bibliometric analysis from its first publication, Endocrinol Res Pract. 2024;28(2):65-70.

DOI: 10.5152/erp.2024.23410

gland" OR "epiphysis cerebri" OR "pineal body" OR "conarium" in all fields in advanced search. The search guery was "pineal body" OR "pineal gland" OR "epiphysis cerebri" OR "conarium." First of all, original articles were selected from the document types category of WoS. Reviews (1308), proceedings (731), meeting abstracts (451), notes (139), book chapters (90), editorial materials (73), letters (67), early access (32), book reviews (6), and other document types were excluded. All data from 1976 to 2023 were included. For the remaining articles, publication dates, journals in which they were published, country, affiliated journals, keyword frequency, trend author keywords, and the most cited articles on the pineal gland were determined. All the articles on the pineal gland in WoS downloaded through this search method (access date: 21.11.2023) were analyzed bibliometrically by VOSviewer (Version 1.6.13, Leiden University: Centre for Science and Technology) package program.⁹ The search strategy diagram can be appreciated in Figure 1.

Statistical Analysis

In the search conducted on the WoS database, a total of 11100 results were obtained. This study performed the bibliometric analysis of only 8719 publications that were in the article category. The relationships between the data, such as authors, citation, journal, country, institution, and keywords, were visualized using VOSviewer (Version 1.6.15). The minimum number of occurrences of determined keywords was chosen as "3" while the keyword-creating map was designed on VOSviewer. Using this software, it was found that there were 1872 different relevant keywords in these articles. Then the categorical data are presented as frequency and percentage.

Results

A total of 11100 publications were obtained through literature review. The 10 most popular document types are as follows: Articles (8719), reviews (1308), proceeding papers (731), meeting abstracts (451), notes (139), book chapters (90), editorial materials (73), letter (67), early access (32), and book review (6) (Figure 2A). Most of them were original articles (78.55%). Of these articles, 97.09% (10770) were written in English. Other articles were written in French (85), Spanish (76), Russian (51), German (36), Polish (26), Japanese (11), Turkish (11), Portuguese (10), Chinese (4), Czech (4), Dutch (2), Hungarian (2), Italian

MAIN POINTS

- · Bibliometric analysis can help researchers gain information on trends and rare studies for a particular topic.
- · We think that the use of keyword analysis is advantageous to the research of hotspots in the field of the pineal gland.
- The bibliometric studies on the pineal gland are limited. One of them analyzed the studies on the pineal gland about melatonin between 1966 and 1994. The other one focused on all pineal gland studies between 1978 and 1994. We think that the use of keyword analysis is advantageous to the research of hotspots in the field of the pineal gland.
- Both studies examined studies up to the end of 1994. Our study includes all original articles on the pineal gland in the current literature since the first publication of the topic.
- We hope that our study will contribute to the global and current status of the topic in the scientific area and can be considered to have a guiding value for researchers interested in this subject.

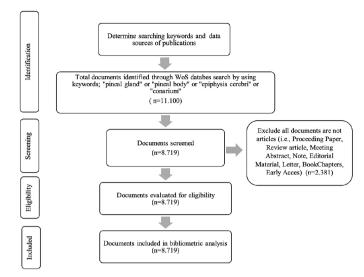


Figure 1. Flow chart diagram for the search strategy.

(2), Ukrainian (2), and Unspecified (1). The first studies on the pineal gland were in the 1970s. The first publication was written by Davis WH, in 1976, and took part in the Davis WH, Journal of Thought, 1976.

The first studies on the pineal gland were conducted in 1976. The highest number of publications on the pineal gland was in 1994 (335 studies), and the lowest number was in 1976 (1 study). The number of articles published between 1976 and 1990 was quite low. Considering the average number of articles in all years (mean standard deviation: 193.75 ± 93.16 articles), it was seen that the number of articles published between 1991 and 2011 was above the average. Between 2012 and 2023, the number of publications remained below

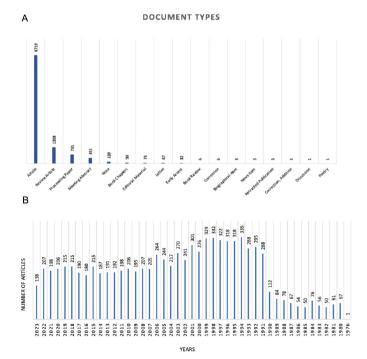


Figure 2. Overview of publications on the pineal gland. (A) Distribution of the document types and language. (B) Distribution of articles on pineal gland according to years.

average in 2012, 2013, 2014, 2016, 2017, and 2023, and remained above normal in the remaining years. In addition, after the first article in the field about the gland, which was published in 1976, no original article was published for the next 3 years. Figure 2B shows the distribution of articles on the pineal gland according to years.

Active Authors and Institutions

The top 10 authors who produced the highest number of articles related to the PG were as follows: Reiter, Russel J. (280); Klein, David C. (122); Guerrero, Josep M. (94); Pevet, Paul (92); Moller M. (89); Vollrath, Lutz (85); Pévet P. (83); Haldar C. (79); Korf, Horst (68); and Simonneaux V. (66) (Figure 3A).

The top 10 institutions that produced the highest number of articles concerning the pineal gland were as follows: Centre National De La Cherche Scientifique CNRS (351), University of Texas System (346), University of Texas Health Science Center at San Antonio (283), National Institutes of Health (NIH) USA (254), Universite de Strasbourg (193), Universites de Strasbourg Etablissements Associes (193), Universidade de Sao Paulo (158), Udice French Research Universities (157), University of California System (147), and NIH Eunice Kennedy Shriver National Institute of Child Health Human Development (NICHD) (135).

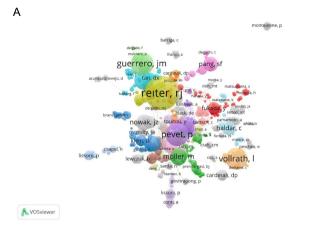
Popular WoS Categories and Active Research Areas

The pineal gland is covered by 165 WoS categories. The number of articles was refined as follows according to the popular 10 categories of WoS: Neurosciences (2878), Endocrinology Metabolism (1922), Physiology (1646), Biochemistry Molecular Biology (972), Cell Biology (604), Clinical Neurology (580), Pharmacology Pharmacy (557), Biology (556), Zoology (444), and Medicine Research Experimental (381).

Furthermore, the most popular 10 active research areas, out of a total of 113 fields were as follows: Neurosciences Neurology (3268), Endocrinology Metabolism (1931), Physiology (1,646), Biochemistry Molecular Biology (1012), Cell Biology (607), Pharmacology Pharmacy (591), Life Sciences Biomedicine Other Topics (556), Zoology (450), Research Experimental Medicine (381), and Science Technology Other Topics (334). Anatomy and morphology studies (239), although popular, were ranked 13th.

Productive Countries

A total of 113 countries had produced publications. The most active 10 countries were the United States (2451), Japan (738), France (683), Germany (646), Spain (614), PR China (537), Italy (397), India (387),



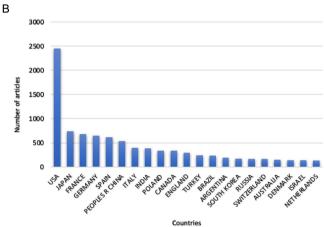


Figure 3. Analysis of publications and countries on the pineal gland. (A) Network visualization map for cluster analysis based on active authors on the pineal gland. (B) Distribution of the productive countries that produced more than 100 articles.

Poland (339), and Canada (336) when the studies were refined by country. Furthermore, the productive countries that produced more than 100 articles are shown in Figure 3B.

Active Journals

Articles were published in a total of 500 journals. Of them, 10 were published with more than 10 articles. Those are shown in Figure 4. It

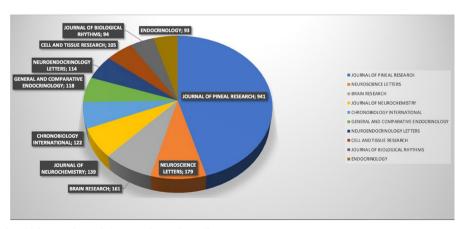


Figure 4. The most active 10 journals and the number of studies.

Table 1. The Most Cited Top 10 Studies and the Citation Numbers

Article	Citation number	Average citation per year
Shughrue et al ¹⁰	1893	70.11
Brainard et al ¹¹	1213	52.74
Barlow & Dietz ¹²	1016	39.08
Reiter ¹³	753	25.97
Dubbels et al ¹⁴	745	25.69
lliff et al ¹⁵	660	60.00
Davis et al ¹⁶	629	27.35
Walther & Bader ¹⁷	549	26.14
Lyssenko et al ¹⁸	548	36.53
Barlow-Walden et al ¹⁹	508	17.52

was seen that most of the articles were published in Journal of Pineal Research (ISSN: 0742-3098) which provides a forum for original research involving any aspect of the pineal gland or its hormonal products, with a focus on melatonin and its role in sleep and circadian rhythms. The journal with the largest number of original papers followed by Neuroscience Letters and Brain Research.

Citation Analysis

A total of 260 181 citations were recorded in the WoS database for studies on the pineal gland between 1970 and 2023. The 10 most cited studies, along with the number of citations and the average citation count per year, are given in Table 1.10-19

Keyword Analysis

To create a high-quality, systematic search, relevant keywords must be identified and incorporated into the search strategy. For an effective search plan, the relationship between keywords in research articles should be strong.²⁰ It was determined that the most popular keywords in the articles were pineal gland, melatonin, circadian rhythm, rat, retina, photoperiod, circadian, aging, serotonin, oxidative stress, and brain. The most commonly used keyword in the studies was "melatonin." Also, the rare topics related to pineal gland studies were stated as follows: noradrenaline release, preeclampsia, Lewis rat, pineal parenchymal tumors, human pineal, chaos, brain neoplasms, senile dementia, and epithelial-to-mesenchymal transition. The popular keyword map associated with the studies of pineal glands is shown in Figure 5.

Discussion

In the current study, in which we analyzed the global research output on the pineal gland, the results indicated the researchers' interest in the gland and provided quantitative data about its place in the scientific area. It was seen that 260 181 citations were made in the WoS database for studies on the pineal gland, and articles associated with the pineal gland were published in a total of 500 journals, 113 fields, and within 165 WoS categories. It seems that the gland has been investigated in various categories and fields through numerous studies.

The productivity of publications can be directly associated with the economic size and opportunities of the prolific countries.⁶ According to results in WoS, the United States leads international scientific production on the pineal gland, although the institution that produces

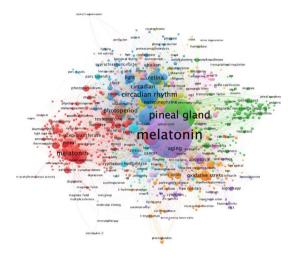


Figure 5. Network visualization map for cluster analysis based on keyword analysis on the pineal gland.

the most papers on the gland is the Center National de La Cherche Scientifique (CNRS) in France. As a journal in the USA, Journal of Pineal Research is the journal where the studies in this field are published the most, but it was seen that the most cited studies are in other journals. In terms of citation numbers, only one study in the top 10 list was published in Journal of Pineal Research. This particular study by Dubbels et al is not directly a study on the pineal gland but also more related to melatonin biochemistry.¹⁴ As seen in the keyword cluster map, generally, it seems that melatonin research is currently the major prime mover in pineal research, overcoming all research on other aspects of the pineal gland.

Citations are the indicators of academic success for authors and journals. Identifying the most cited articles is very important in terms of accessing quality articles on that subject.²¹ The study by Shughrue et al¹⁰ on the comparative distribution of estrogen receptors (α and β mRNA) is the most referenced study in WoS about the field of the pineal gland. Shuughrue et al's¹⁰ article was determined to receive the highest total number of citations per year as well as the highest average number of citations when citation analysis was performed. The Journal of Comparative Neurology published the study. In the WoS database analysis, this paper has received the highest citations; however, the publication is not among the top 10 journals with the greatest number of studies on the pineal gland when compared to data gathered from journals. We can infer that this is because there are 500 active publications and a broad spectrum of fields related to the pineal gland.

Multidisciplinary research enables the interdisciplinary exchange of ideas, the learning of new skills, and higher-quality results.²² There has been a trend away from mono-disciplinary research toward multidisciplinary forms of research in recent years.²³ Category analysis shows that Neurosciences, Endocrinology Metabolism, Physiology, Biochemistry Molecular Biology, Cell Biology, Clinical Neurology, Pharmacology, Biology, Zoology, and Experimental Medicine Research are the main categories for the pineal gland studies in WoS. It was seen that the pineal gland is included in many categories; this could be a result of the fact that the pineal gland is an interdisciplinary study topic. When the number of articles published since 1990,

excluding the years 2012, 2013, 2014, 2016, and 2017, is examined, the regular publication above the publication average shows that the topic is a focus of curiosity in many fields.

In our research on the pineal gland, it has been observed that many different fields of knowledge, both basic and clinical, come together. Therefore, the journals most frequently used by pineal researchers for publication will be those with multidisciplinary content. In our study, the 10 journals with the most publications on the pineal gland are as follows: Journal of Pineal Research, Neuroscience Letters, Brain Research, Journal of Neurochemistry, Chronobiology International, General and Comparative Endocrinology, Neuroendocrinology Letters, Cell and Tissue Research, Journal of Biological Rhythms, and Endocrinology. All these journals have multidisciplinary content.

The keywords that are used by indexing systems, such as search engines, databases, and library catalogs, can identify the most suitable matches for a search. Also, keywords play an important role in the detectability of academic articles and how they are found.²⁴ The use of keyword analysis is beneficial to the study of hotspots in the field of the pineal gland. Keyword analysis results of pineal gland articles show that the most used keywords from the past to the present include pineal gland, melatonin, circadian rhythm, rat, retina, photoperiod, circadian, aging, serotonin, oxidative stress, and brain. With the keywords used in articles about the pineal gland to date, it has been seen that the pineal gland is included in many disciplines and that studies are showing different approaches in terms of subject and content.

The focus of five recently added original articles on the pineal gland to WoS was determined as the pineal cysts in children and the pineal gland hormone melatonin as a potential biomarker for various cancers.^{25,26} The age-related gross and histomorphological dynamics of the pineal gland associated with melatonin and its effects on the liver are discussed by some of the authors.^{27,28} Also, another study focuses on the effects of pineal germinoma, upward gaze paralysis, and diabetes insipidus.29

The WoS database is considered more reliable than other databases. Other databases, like PubMed and Scopus, were left out of our analysis because the WoS database has the greatest quantity of publications and citations. Furthermore, every journal included in the WoS index has a high impact factor.^{30,31} It provides access to articles on the subject in the best journals in the field for researchers who want to learn about the pineal gland. For this reason, databases such as PubMed and Scopus were not used in our study, but the WoS database was used.

As far as we know, the present research is the first bibliometric study to provide a comprehensive analysis of scientific publications with an emphasis on the pineal gland since 1976. This study provides a comprehensive summary of 8719 articles related to the pineal gland indexing in WoS until November 21, 2023. In addition, the most interesting and cited journals related to the pineal gland were included. Trending topics studied in conjunction with the pineal gland were presented. The comprehensive analysis and findings of this study can be considered to have a guiding value for researchers interested in this subject.

The main limitation of our study is that we emphasized on published journal articles only from the WoS database. Therefore, journals from non-English speaking countries might be underestimated. In addition, only articles were included, and other types were not included

in the analyses. The citation analysis did not take into consideration the self-citations, which could create a bias in the number of citations for countries, journals, and authors.

Ethics Committee Approval: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.T., E.S., S.N.S.; Design - B.T., E.S., S.N.S.; Supervision - B.T.; Resource - E.S., S.N.S.; Materials - E.S., S.N.S.; Data Collection and/or Processing - E.S., S.N.S.; Analysis and/or Interpretation - E.S., S.N.S.; Literature Search – E.S., S.N.S.; Writing – B.T., E.S., S.N.S.; Critical Review

Declaration of Interests: The authors have no conflicts of interest to

Funding: This study received no funding.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

- Samuel DS, Duraisamy R, Kumar MP. Pineal gland-A mystic gland. Drug Invent Today. 2019;11(1):55-58.
- López-Muñoz F, Marín F, Álamo C. History of pineal gland as neuroendocrine organ and the discovery of melatonin. Melatonin Neuroprotective Agents Antidepressant Ther. 2016:1-23.
- Sharma DK, Sharma V, Sinha B, et al. Pineal gland' still a bit of mystery: an escort study. IJA. 2015;4(3):133-140. [CrossRef]
- Gheban BA, Rosca IA, Crisan M. The morphological and functional characteristics of the pineal gland. Med Pharm Rep. 2019;92(3):226-234.
- López-Muñoz F, Molina JD, Rubio G, Alamo C. An historical view of the pineal gland and mental disorders. J Clin Neurosci. 2011;18(8):1028-1037. [CrossRef]
- Golpinar M, Demir E. Global research output of the cerebellum: yesterday, today, and tomorrow. J Anat Soc India. 2020;69(3):155. [CrossRef]
- Bahşi İ, Adanır SS, Kervancıoğlu P, Orhan M, Govsa F. Bibliometric analysis of Turkey's research activity in the anatomy and morphology category from the Web of Science database. Eur J Ther. 2022;27(4):268-280. [CrossRef]
- Kiraz M, Demir E. A bibliometric analysis of publications on spinal cord injury during 1980-2018. World Neurosurg. 2020;136:e504-e513. [CrossRef]
- Van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010;84(2):523-538. [CrossRef]
- 10. Shughrue PJ, Lane MV, Merchenthaler I. Comparative distribution of estrogen receptor-alpha and -beta mRNA in the rat central nervous system. J Comp Neurol. 1997;388(4):507-525. [CrossRef]
- 11. Brainard GC, Hanifin JP, Greeson JM, et al. Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. J Neurosci. 2001;21(16):6405-6412. [CrossRef]
- Barlow SE, Dietz WH. Obesity evaluation and treatment: expert committee recommendations. The Maternal and Child Health Bureau, Health Resources and Services Administration and the Department of Health and Human Services. Pediatrics. 1998;102(3):E29. [CrossRef]
- Reiter RJ. Oxidative processes and antioxidative defense mechanisms in the aging brain. FASEB J. 1995;9(7):526-533. [CrossRef]
- 14. Dubbels R, Reiter RJ, Klenke E, et al. Melatonin in edible plants identified by radioimmunoassay and by high-performance liquid chromatography-mass spectrometry. J Pineal Res. 1995;18(1):28-31. [CrossRef]
- 15. Iliff JJ, Lee H, Yu M, et al. Brain-wide pathway for waste clearance captured by contrast-enhanced MRI. J Clin Invest. 2013;123(3):1299-1309. [CrossRef]

- 16. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. J Natl Cancer Inst. 2001;93(20):1557-1562. [CrossRef]
- 17. Walther DJ, Bader M. A unique central tryptophan hydroxylase isoform. Biochem Pharmacol. 2003;66(9):1673-1680. [CrossRef]
- 18. Lyssenko V, Nagorny CLF, Erdos MR, et al. Common variants in MTNR1B are associated with an increased risk of type 2 diabetes and impaired early insulin secretion. Nat Genet. 2009;41(1):82-88. [CrossRef]
- Barlow-Walden LR, Reiter RJ, Abe M, et al. Melatonin stimulates brain glutathione peroxidase activity. Neurochem Int. 1995;26(5):497-502. [CrossRef]
- 20. Buchanan H, Grimmer K. Keyword parsimony—lessons from a scoping review. Syst Rev. 2021;10(1):230. [CrossRef]
- 21. Tekin AM, Bahşi İ, Bayazit YA, Topsakal V. Global research on hereditary hearing impairment over the last 40 years: a bibliometric study. Int Adv Otol. 2021;17(6):482-491. [CrossRef]
- Medhi B, Bansal S, Mahendiratta S, Kumar S, Sarma P, Prakash A. Collaborative research in the modern era: need and challenges. Indian J Pharmacol. 2019;51(3):137-139.
- Dalton A, Wolff K, Bekker B. Multidisciplinary research as a complex system. Int J Qual Methods. 2021;20:160940692110384. [CrossRef]
- Corrin L, Thompson K, Hwang G, Lodge JM. The importance of choosing the right keywords for educational technology publications. AJET. 2022;38(2):1-8. [CrossRef]

- 25. Szathmari A, Vasiljevic A, Di Rocco F, Beuriat PA, Mottolese C. Pineal cysts in children: a pediatric series treated over the last twenty years in Lyon. Childs Nerv Syst. 2023;39(12):3467-3474. [CrossRef]
- 26. Jayaraman S, Rajarathinam T, Jang HG, et al. Ruthenium-anchored carbon sphere-customized sensor for the selective amperometric detection of melatonin. Biosensors. 2023;13(10):936. [CrossRef]
- 27. Hussain M, Kausar R, Qureshi AS, Jamil H. Age-related gross and histomorphometric dynamics of the pineal gland (epiphysis cerebral) associated with melatonin profile in beetle goat (Capra aegagrus hircus) of Pakistan. Pak Vet J. 2023;43(3):531-536.
- Lee R, Lee WY, Park HJ. Effects of melatonin on liver of D-galactoseinduced aged mouse model. Curr Issues Mol Biol. 2023;45(10):8412-8426. [CrossRef]
- 29. Karimifar M. Pineal germinoma presented with paralysis of upward gaze and diabetes insipidus. Acta Endo (Buc). 2023;19(1):99-103.
- Demir E, Yaşar E, Özkoçak V, Yıldırım E. The evolution of the field of legal medicine: a holistic investigation of global outputs with bibliometric analysis. J Forensic Leg Med. 2020;69:101885. [CrossRef]
- 31. Doğan G, Kayır S. Global scientific outputs of brain death publications and evaluation according to the religions of countries. J Relig Health. 2020;59(1):96-112. [CrossRef]