

Analysis of “Intracytoplasmic sperm injection” titled studies with science mapping method

“Intracytoplasmic sperm injection” başlıklı çalışmaların bilim haritalama yöntemi ile analizi

Yasemin Yüksel

Uzm.Dr. Üremeye Yardımcı Tedavi Merkezi, Kadın Hastalıkları ve Doğum Kliniği, Ankara Şehir Hastanesi, Ankara, Türkiye, dryuksely@gmail.com. 0000-0003-3343-7957

ABSTRACT

Aim: Intracytoplasmic sperm injection (ICSI) is the most commonly used assisted reproductive technology method in the treatment of infertility, especially for the severe male factor infertility. This study aimed to determine the inclusive structure of articles about ICSI, the evolution of research themes, the research tendencies and their geographical distribution. Bibliometric science mapping was used for this purpose. **Materials-Methods:** Within the scope of the research, the WoS database was examined and a total number of 2379 articles, matching the search criteria, were analyzed. Studies in the data set were in terms of journals, researchers, related topics and countries. **Results:** It has been determined that the first article about ICSI was published in 1993, a serious increase in the number of articles was observed until 1998 and the largest number of articles were published in 2021. The most influential author in this field in terms of number of publications and citations was found as a Belgian researcher “Prof. Paul Devroey (Free University of Brussels)” and Belgian researchers were found to be in the first place. “Human Reproduction” is the most influential journal in this field in terms of citations and indexing. “IVF”, “Pregnancy” and “Infertility”, are the most commonly used words along with ICSI. The study named “High fertilization and implantation rates after intracytoplasmic sperm injection” is the most cited study. The USA ranked first in the number of single-country, multi-country and total publications. China, Belgium, Turkey and Italy are also among the leading countries. When the publications are examined in terms of cooperation between countries, it is seen that the joint publications are most commonly conducted between Italian-Spain and Dutch-Belgian academics. **Conclusion:** It is considered that the results of this study will raise awareness about ICSI and shed light on researchers.

ÖZ

Amaç: İntrasitoplazmik sperm enjeksiyonu (ICSI), şiddetli erkek faktörlü kısırlık başta olmak üzere infertilite tedavisinde kullanılan en yaygın yardımcı üreme teknolojisi yöntemidir. Bu çalışma ile ICSI konusundaki yayınların kapsayıcı yapısının, araştırma temalarının evriminin, araştırma yönelimlerinin ve coğrafi yayılımının belirlenmesi amaçlanmıştır ve bu doğrultuda bibliyometrik bilim haritalama kullanılmıştır. Gereç-Yöntem: Araştırma kapsamında WoS veri tabanı incelenmiş ve arama kriterlerine uyan 2379 makale analize tabii tutulmuştur. Veri setindeki çalışmalar; dergiler, araştırmacılar, ilişkili konular ve ülkeler açısından incelenmiştir. Bulgular: ICSI konusunda ilk makalenin 1993 yılında yayınlandığı, 1998 yılına kadar makale sayısında ciddi bir artış eğilimi olduğu ve en çok 2021 yılında üretildiği tespit edilmiştir. Yayın sayısı ve atıfları açısından bu alanda en etkili yazarın Belçikalı araştırmacı “Prof.Dr. Paul Devroey (Free University of Brussels)” olduğu, Belçikalı araştırmacıların ilk sıralarda yer aldığı bulunmuştur. “Human Reproduction”, atıf ve indeksleri açısından bu alanda en etkili dergidir. “IVF”, “Pregnancy” ve “Infertility”, ICSI ile birlikte en sık kullanılan kelimelerdir. “High fertilization and implantation rates after intracytoplasmic sperm injection” isimli çalışma en fazla atıf alan çalışmadır. Tek ülkeli, çok ülkeli ve toplam yayın sayısında ABD ilk sırada yer almış olup; Çin, Belçika, Türkiye ve İtalya önde gelen ülkeler arasındadır. Ülkeler arası işbirliği açısından bakıldığında ise en sık İtalya-İspanya ve Hollanda- Belçika kökenli akademisyenler arasında ortak yayın yapıldığı görülmektedir. Sonuç: Bu çalışma sonuçlarının, ICSI hakkında farkındalık oluşturacağı ve araştırmacılara ışık tutacağı değerlendirilmektedir.

ARTICLE INFO/MAKALE BİLGİSİ

Key Words: Intracytoplasmic sperm injection, ICSI, Infertility, Bibliometric Analysis, Science Mapping

Anahtar Kelimeler: İntrasitoplazmik sperm enjeksiyonu, ICSI, Infertilite, Bibliyometrik Analiz, Bilim Haritalama

DOI: 10.5281/zenodo.7312835

Corresponding Author/Sorumlu Yazar: Uzm.Dr. Üremeye Yardımcı Tedavi Merkezi, Kadın Hastalıkları ve Doğum Kliniği, Ankara Şehir Hastanesi, Ankara, Türkiye, dryuksely@gmail.com.

Received Date/Gönderme Tarihi: 21.10.2022

Accepted Date/Kabul Tarihi: 11.11.2022

Published Online/Yayımlanma Tarihi: 31.12.2022

INTRODUCTION

The frequency of infertility problem has been increasing all over the world recently. Assisted reproductive techniques can be preferred after using pharmacological agents according to the cause of infertility and the characteristics of the patients. In vitro fertilization (IVF) is the only option for infertile patients who cannot become pregnant with the vaccination method or in male factor infertility for whom vaccination is not suitable.

IVF was first introduced to the world in the 1970s for use in female patients with tubal damage. There are two different techniques as conventional IVF and Intracytoplasmic sperm injection (ICSI). Until 1992, the term IVF was perceived as a conventional IVF technique and commonly used in assisted reproductive technologies. Then, the ICSI method has begun to replace the classical IVF method due to the inadequacy of conventional IVF especially in patients with male factor and fertilization failures ICSI (1).

ICSI is a widely used fertilization method that involves the injecting a single sperm into the cytoplasm of an oocyte by using a glass micropipette (2). This method was introduced in 1992 to improve fertilization in couples with male factor infertility undergoing in vitro fertilization or in couples who had fertilization failure in a previous IVF cycle without detectable abnormalities in semen parameters (3). Ovarian stimulation, egg retrieval and embryo transfer are performed in ICSI as in conventional IVF. The main difference compared to the conventional IVF method is the injection of a single sperm cell into the egg cell as an additional step after the oocytes are cleared of granulosa cells by denudation (4).

ICSI, which accounts for almost 70% of approximately 2.8 million assisted reproductive technology cycles annually, has become the most common laboratory technique in assisted reproductive technology in order to overcome the severe male factor infertility although it is promoted as a modification of traditional IVF treatment. The high success rate of ICSI is a result of its increased use, especially in non-male factor infertility. The use of ICSI varies considerably according to the region. While ICSI was used in 69% of IVF cycles in 2012 in Europe, the use of ICSI in IVF cycles in the USA increased from 34% to 76% between 1996 and 2012. The greatest increase was documented in non-male factor infertility, where ICSI use increased from 15% to 67% over this time period (5). The latest report of the European IVF Monitoring Consortium showed that ICSI was used in 71.3% of fresh treatments in 2014, which is slightly more than the previous year (6). When evaluated in terms of general assisted reproductive technology cases; ICSI method constitutes almost all of cases in the Middle East, and 85%, 74%, 70% and 55% in Latin America, North America, Europe and Asian countries, respectively (2,7,8).

The reason for this excessive use is becoming of ICSI as an acceptable method for the treatment of female infertility in cases of polyspermia or low fertilization, where oocytes are degraded in quality or number. The requested indication for the use of ICSI in the absence of an identifiable male factor include; unexplained infertility, poor quality oocytes, low oocyte reserve, advanced maternal age, lack or failure of previous fertilization with conventional in vitro fertilization, preimplantation genetic diagnosis, fertilization after in vitro maturation and fertilization of cryopreserved oocytes. Recently, routine use of ICSI is recommended in all IVF cases without indication in many centers. The rationale for all these indications, except for PGT, is to avoid fertilization failure. At the same time, ICSI is a technique that requires more labor and technical procedures and costs more than conventional IVF. While ICSI is used in these

environments due to unresolved concerns about the health conditions of newborn after ICSI, the probability of fertilization failure in patients must be balanced with the possible risks and costs of the procedure (9-11).

Traditional IVF can be a more suitable technique than ICSI in cases of non-male factor infertility (for example, tubal disease, ovulation disorder or unexplained infertility), which accounts for approximately 60% of primary assisted reproductive technology (12). The use of ICSI for conditions other than severe male-factor infertility has raised questions about both the safety and efficacy of this technique. Early studies about the success rates and safety of ICSI showed that the live birth rates are comparable with IVF. Although ICSI is a safe method, has caused some minor increases in congenital abnormalities in children (7). Potential risks for offspring, including an increased risk of non-chromosomal birth defects, chromosomal abnormalities, and epigenetic syndromes, have been identified after ICSI (13). The advantages and disadvantages of IVF and ICSI should be well defined in the presence of less severe male factor infertility or other infertility diagnoses. Because traditional IVF application should be preferred if there is neither advantage nor additional risk of using ICSI (14). It has become a problem to believe that ICSI, which helps to overcome severe male factor infertility, can be a panacea for all infertile patients (15).

The information obtained about any study is increasing day by day. The information obtained is related to other disciplines over time. It is not easy to obtain meaningful results and to identify study orientations and tendency with classical methods in this heap of information and complex environment. New research methods are needed in order to examine the study area with a holistic perspective and to shed light on new studies.

The concept of bibliometrics can be expressed as the mathematical and statistical quantitative analysis of works produced by individuals or institutions in a certain field, period and region and the relations between them. It is academically important to determine the studies carried out in any field, their development and changes during the process, and possible tendencies (16).

Nowadays, the importance of correct analysis of data has especially increased as the literature has become extremely comprehensive. This is where bibliometric methods become a part of the activity. Bibliometric methods are used to analyze large volumes of data in the literature.

The analyzes include information about a scientific discipline, the study subject, academic institutions, countries, authors, cooperation between authors (17-18).

Science mapping is a methodology that combines quantitative analysis, classification and visualization to determine composition and interrelationships between bibliographic objects (19).

Our study aimed to determine the inclusive structure of articles about ICSI, the evolution of research themes, the research tendencies and their geographical distribution. Bibliometric science mapping was used for this purpose.

MATERIAL AND METHOD

Research Framework

The research framework of the ICSI study topic is presented in Figure 1. A database containing qualified data has been selected in order to perform bibliometric analysis of the ICSI subject. For this purpose, the Web of Science Core Collection (WoS) database, which is academically accepted, was preferred. This database is the most frequently used scientific information source in the world (20).

After the selection of the data set, the data were filtered. Filtering was applied in the database in the form of “Intracytoplasmic Sperm Injection” OR “ICSI” headings in a search of the WoS database on July 14, 2022.

When the “Article and Review Articles” document types on ICSI were selected in the database, 4035 articles were reached. The language option was determined as English and 3906 articles were obtained. A total of 2464 studies were obtained when only “Obstetrics Gynecology” is selected in the Web of Science Categories.

Finally, since the processes of the articles have been continuing in 2022, articles for the year 2022 were also excluded from the review, and as a result, 2379 articles were studied.

Bibliometric Analysis

Bibliometrix program was used to perform bibliometric analysis of the data obtained from WoS. Bibliometrix is open source software written in R. It is one of the most commonly used programs for scientific literature mapping (21).

The reviewed articles were analyzed in two parts. In the first part, the general analysis of the articles, and in the second part, the content analysis was made.

In the first part, articles, journals, researchers and institutions on ICSI and the countries where the studies were conducted were examined. h, g and m indexes were calculated within the scope of the examinations.

In the second part, the intellectual structure of the ICSI subject was analyzed through content analysis. In content analysis, word analyzes and co-occurrence networks and citation analyzes were used. The focus, main topics and thematic development levels of the researches were determined with the intellectual structure analysis and international cooperation networks and international cooperation were examined.

General Analysis of Articles

The H-index or Hirsch index was created by Jorge Hirsch in 2005. If an author has X articles that have been cited at least X times by other authors, the author’s h-index is equal to X (22). The G-index was created by Leo Egghe in 2006. The H-index does not use the average of the number of citations to measure the citation performance of an article. The G-index was developed to fix this shortcoming. Contrary to the H-index, highly cited articles have drawn attention (23).

While evaluating the academic success of young scientists; the fact that their articles did not have enough time to be cited is not taken into account. This is one

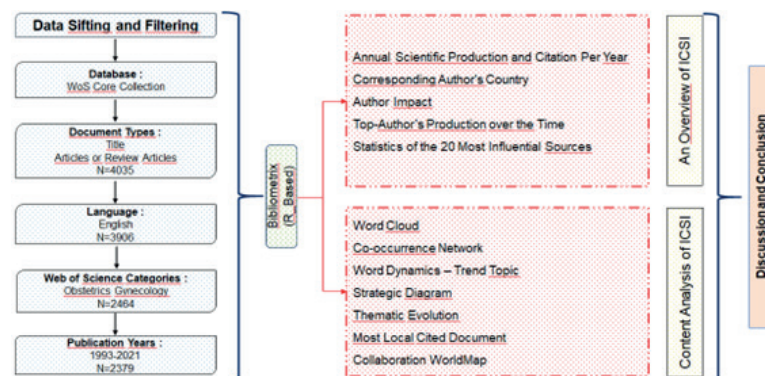


Figure 1. Workflow of science mapping

of the criticisms about the h-index. Impact factor can be a realistic criterion. One way to compare academic histories of different lengths is to compare the h-index to years of active academic study. This index developed by Hirsch, just like the h-index, is called the m-index (24).

Content Analysis of Articles

A word cloud of the keywords of the articles on ICSI was created with the Bibliometrix method within the scope of content analysis. The word cloud is a graphical display of current headings about the ICSI topic. Different correlation areas and the most dominant terms can be determined with the help of the word cloud (25).

Thematic mapping

Thematic mapping reveals the temporal dynamics of research areas. The thematic development of ICSI researches including the time interval between 1993 and 2021 is analyzed from a dynamic perspective.

The research period (1993-2021) was divided into four successive sub-periods. The first sub-period was determined as 9 years (1993-2001) due to limited publications in the early years. The second, third and fourth sub-periods were divided into time intervals as 8 years (2002-2009), 7 years (2010-2016), and 5 years (2017-2021) and included in the analysis.

Thematic mapping was performed with word analysis in the Bibliometrix program, and strategic diagrams were created. Keywords of the articles are used in word analysis. The keywords of the articles are determined by the authors and are chosen from the words that will best represent the article. Since the keywords represent the article, dynamics related to the study subject can be determined by performing keyword analysis (26).

The strategic diagram reflects the interaction of actors in a research area over a period of time. It is a static description of the network structure of a scientific field. Çeşitli konfigürasyonların zamansal dinamiklerini veya aynı zaman diliminde ağlar arasındaki etkileşimleri analiz ederek, değişen daha derin düzeyde ortaya çıkarılabilir (27).

The most repeated keywords are shown as theme clusters in the word analysis. The first 250 keywords were used in the analysis. The words in the clusters are the keywords with the highest frequency of use in the cluster. The size of the clusters reflects the frequency of use of keywords.

The sub-periods are divided into four periods. Each period shows different themes and two criteria were used to scale the periods, namely the theme clusters. These are centrality and density. Density and centrality constitutes the y-axis and x-axis of the thematic map,

respectively. The centrality grades the importance and the intensity grades the development of the chosen theme (28-30).

- “Motor Themes”, is the first quarter theme. It forms the upper right part. It expresses high density and centrality. Keywords in this theme have strong interlinks (30).
- “Highly Developed and Isolated Themes”, is the second quarter theme. It forms the upper left part. This theme expresses higher density and lower centrality. They are important for the development of the study subject (30).
- “Emerging or Declining Themes”, is the third quarter theme. It forms the lower left part. They are emerging or decreasing themes. It is a theme with low centrality and intensity (30).
- “Basic and Transversal Themes”, is the fourth quarter theme. It forms the lower right part. It has low density and high centrality. The keywords in this theme have strong inner links. This theme includes words that are frequently repeated and have strong associations. (30).

Thematic Evolution Map

The Sankey Diagram was used to construct the thematic evolution map. In this diagram, each junction represents a set of themes. The size of the nodes is directly proportional to the number of keywords. Flow lines between nodes point to the direction of evolution of theme clusters over time. The edge width of the node is the sum of the connected elements. Sankey diagrams show the flows within a process and in this case help to review the process. They are frequently used in industrial processes and engineering (31).

Citation Analysis

The development dynamics of research topics can be examined with citation analysis. In our study, citation analysis was performed to analyze the articles about ICSI and their relationships. Local Citations: can be defined as the number of citations to an article by the articles in the dataset used. The Global Citation shows the number of citations made to the article from the WoS core database. It is necessary to eliminate the effect of time from citation analysis. Because newly published articles do not have enough time to be cited. Bu etkiyi gidermek için Annual Local Citations (LC/YYP) and Annual Global Citations (GC/YYP) parameters can be used to remedy this effect (32).

RESULTS

Overview

It is seen that the first study about the ICSI study subject was performed in 1993. The number of authors in the aforementioned 2379 articles is 7884, and the number

of single-authored studies is 48. While the number of studies per author is 0.302, the number of authors per study is 3.31 and the collaboration index is 3.38.

Annual Scientific Production and Citation Per Year

Annual scientific production and annual average citations on ICSI between 1993-2021 were obtained using Bibliometrix as shown in Figure 2. It is seen that the number of articles in the field of ICSI increased very rapidly from 1993 to 1998. While the number of articles produced in 1993 was 3, the total number of articles produced annually became 108 after 5 years. The annual number of articles produced between 1998 and 2021 remained almost stable between 67-113. The highest annual number of articles was reached in 2021 (n=113).

The trend line, the trend line equation and the R²-confidence coefficient were added to the annual scientific production numbers graph in our study. The reliability coefficient value in our study was 0.38, far from 1. This situation was caused by the fact that the annual production number trend in the first years could not be caught in recent years. The equation representing the trend line is presented on the graph (Figure 2).

When the average citations per article are examined, the highest annual average number of citations with a value of 20.8 were reached in the articles published in 1993. The annual average number of citations remained stable between 1.7-3.9 in 1994-2021. In 2019, which is the closest year to the present, the average number of citations was 3.3 per year (Figure 2). It can be said that the number of citations of the publications in recent years is significant since it takes time to cite more recent publications.

Country Statistics

ICSI studies were analyzed in terms of countries. The top 20 countries are presented in Table 1. The table is given in order of total publication.

The USA ranked first in the number of single-country publications (218), multi-country publications (35), and total number of publications (253). In total number of publications, China (214) ranks second and Belgium (196) third. In single-country publications, China (197) ranks second and Turkey (177) ranks third. In multi-country publications, Italy (30) ranks second and Belgium (29) ranks third.

The country with the highest MCP ratio, which is defined as multi-country publications dcasts divided by the total number of publications in the country, is Greece (0.30).

Table 1. Top 20 countries in ICSI studies

Country	TPC	SCP	MCP	MCP_Ratio
USA	253	218	35	0,14
China	214	197	17	0,08
Belgium	196	167	29	0,15
Turkey	185	177	8	0,04
Italy	113	83	30	0,27
Netherlands	112	90	22	0,20
Iran	111	101	10	0,09
Germany	105	83	22	0,21
United Kingdom	96	74	22	0,23
France	92	71	21	0,23
Egypt	84	68	16	0,19
Brazil	82	74	8	0,10
Spain	78	61	17	0,22
Japan	65	62	3	0,05
Israel	64	61	3	0,05
Australia	56	51	5	0,09
Canada	50	45	5	0,10
Denmark	46	37	9	0,20
Greece	43	30	13	0,30
Korea	28	28	0	0,00

TPC = Total number of publications by the corresponding author's country, SCP = Single country publications, MCP = Multiple country publications, MCP_Ratio=MCP/TPC

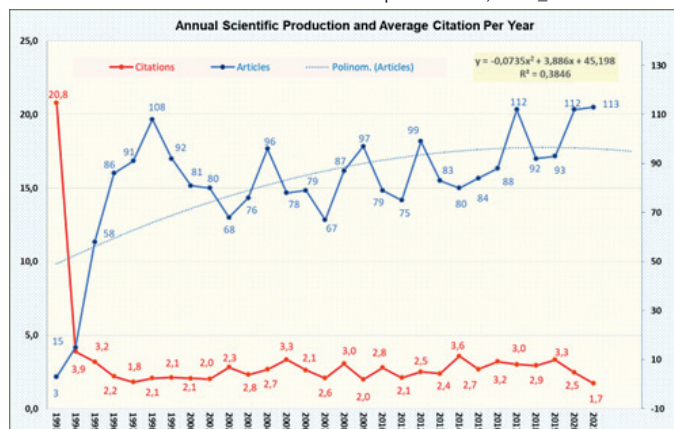


Figure 2. Annual scientific production and citation per year

Author Statistics

Statistics of the top 20 authors, who conducted the most effective studies about ICSI between 1993-2021, are presented in Table 2. The table was created according to the h-index. The h-index, g-index, m-index, total citations (TC), total number of publications (NP), and first year of publication in the ICSI field (PY-baseline) were analyzed for the authors working on the field of ICSI.

The authors with the highest h-index value according to the analysis are Devroey P (57), Tournaye H (42) and Van Steirteghem A (35). The author with the highest G index is Devroey P (57). The author with the highest M-index is Devroey P (1.09). The author with the highest total number of citations is Devroey P (10471) and the author with the highest total number of articles is Devroey P (101). It is possible to say that the most influential author in the field of ICSI is Devroey P.

It is noteworthy that the 20 most influential authors in the field of ICSI started their publication life between 1993-1998. De Sutter P, who have started academic publication life in 2018, draws attention with h-index (20), g-index (27), m-index (0.8), total number of citations (1244) and total number of publications (27).

Figure 3 shows the performance of authors in time who have published articles in the field of ICSI. Considering the length of the article publication line, the authors who published on ICSI for the longest time are Tournaye H (1993-2021), Verheyen G (1994-2021) and Palermo GD (1994-2021).

Table 2. Statistics of the 20 most influential authors in the field of ICSI

Author	h_index	g_index	m_index	TC	NP	PY_start
Devroey P	57	101	1,9	10471	101	1993
Tournaye H	42	75	1,4	5702	76	1993
Van Steirteghem A	35	46	1,346	3662	46	1997
Camus M	34	44	1,133	3993	44	1993
Bonduelle M	33	42	1,138	3426	42	1994
Joris H	28	33	0,933	4161	33	1993
Verheyen G	25	32	0,862	2299	32	1994
Liebaers I	24	27	0,828	2733	27	1994
Dhont M	22	25	0,759	1788	25	1994
Vansteirteghem A	22	24	0,733	2733	24	1993
Diedrich K	21	35	0,75	1248	38	1995
De sutter P	20	27	0,8	1244	27	1998
Nagy ZP	20	21	0,69	1850	21	1994
Palermo GD	20	26	0,714	1694	26	1995
Vansteirteghem AC	20	20	0,667	3931	20	1993
Liu J	18	20	0,621	3077	20	1994
Nagy Z	18	19	0,6	3887	19	1993
Rosenwaks Z	18	24	0,643	1546	24	1995
Tesarik J	17	22	0,586	2094	22	1994
Pellicer A	16	20	0,571	1157	20	1995

Note: NP = Number of publications, TC = Total citations, PY_start = Publication year starting.

The size of the circles in the figure indicates the excess number of articles in that year. Van Steirteghem A reached 16 publications in 1995 and 1998, and became the most published author on ICSI study topic in a year. The opacity of the circles in the figure indicates the total amount of citations that the author has received per year. Van Steirteghem A reached the highest number of citations in 1995 with 88.21 citations. Both the number of publications and annual citations of the authors who published in the 2000s remained low.

Journal Statistics

Articles on ICSI have been published in a wide variety of journals. A total of 2379 analyzed articles were published in 81 different journals. Journals are ranked by h-index to identify the most influential journals in the research field of ICSI.

Table 3 shows the top 20 journals by number of articles. 82.17% (1955/2379) of the total articles were published in these journals. Human Reproduction journal represents 25.85% (615/2379) of the total articles and is the journal with the most publications. The most cited journal about ICSI is Human Reproduction (38665).

Human Reproduction journal, which started its publication life in 1993; is ahead of other journals in terms of h-index (101), g-index (149), m-index (3.37), total number of citations (38655) and total number of publications (615) and is the most influential journal in this field.

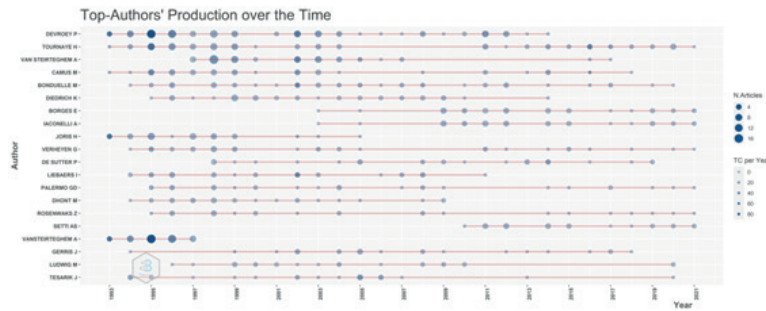


Figure 3. Production of top authors in time

Table 3. Statistics of the 20 most influential journals in ICSI research

Element	h_index	g_index	m_index	TC	NP	TC/NP	PY_start
Human Reproduction	101	149	3,37	38655	615	63	1993
Fertility and Sterility	75	107	2,50	19514	417	47	1993
Reproductive Biomedicine Online	43	64	2,26	5677	192	30	2004
Journal of assisted reproduction and genetics	32	47	1,10	4614	268	17	1994
Human Reproduction Update	26	29	1,00	2812	29	97	1997
European Journal of Obstetrics & Gynecology and Reproductive Biology	20	31	0,80	1163	63	18	1998
Gynecological Endocrinology	16	21	0,67	797	77	10	1999
Molecular Human Reproduction	16	20	0,59	1063	20	53	1996
Archives of Gynecology and Obstetrics	14	24	0,58	681	43	16	1999
Acta Obstetrica et Gynecologica Scandinavica	13	28	0,48	841	30	28	1996
European Journal of Obstetrics Gynecology and Reproductive Biology	11	14	0,42	244	14	17	1997
Gynecologic and Obstetric Investigation	10	17	0,38	303	18	17	1997
Human Fertility	10	14		246	23	11	
International Journal of Fertility & Sterility	9	12	0,60	184	24	8	2008
Journal of Reproductive Medicine	9	13	0,38	219	24	9	1999
Bjog-an International Journal of Obstetrics and Gynaecology	8	12	0,42	345	12	29	2004
Journal of Obstetrics and Gynaecology	8	13	0,50	183	20	9	2007
Clinical and Experimental Obstetrics & Gynecology	7	8	0,44	144	32	5	2007
International Journal of Reproductive Biomedicine	7	11	0,88	125	15	8	2015
Iranian Journal of Reproductive Medicine	7	9	0,44	128	19	7	2007

NP = Number of publications, TC = Total citations, TC/NP = Citations per paper, PY_start = Publication year starting,

In addition, the number of citations per article was also analyzed, showing the ratio between the number of citations and the number of documents for each journal. Human Reproduction Update offers the highest value with an average of 97 citations per article.

It is possible to say that the International Journal of Fertility & Sterility journal, which started its publication life in 2008, has become effective in the field of research quickly when the h index (9), the number of citations (184) and the number of publications (24) of the journal is evaluated.

Content Analysis

In this section, keyword analysis and citation analysis were performed using bibliometric methods to identify the main elements of the ICSI study topic.

Frequency Analysis for Keywords

Bibliometrix was used to obtain data on the keyword frequency (repeat count) of the ICSI study subject and the data are presented in Figure 4. The word cloud is a graphical display of the latest topics in the ICSI workspace. Top 50 emerging keywords preferred by the authors are shown in Figure 4. The size of the keywords

Terms	Frequency
Icsi	858
Intracytoplasmic Sperm Injection	516
Ivf	390
Pregnancy	188
In Vitro Fertilization	178
Infertility	145
Fertilization	134
Male Infertility	107
Pregnancy Rate	100
Azoospermia	92

in the image is directly proportional to the frequency of their appearance in the data set.

The most used keywords are “icsi”, “intracytoplasmic sperm injection” and “ivf”. Besides, derivatives of the “fertility” gain attention in the word cloud. The number of usage of the 10 most used keywords is shown on the left side of the figure.

Keywords Co-occurrence Network

The keywords co-occurrence network is presented in Figure 5. Keywords are clustered in 4 clusters. “icsi” and “intracytoplasmic sperm injection” keywords represent the red and blue cluster, respectively. There is no dominant word in the green and purple clusters.

The strongest links are between “icsi-ivf” and “icsi-pregnancy” in the red cluster. There are also strong links between “intracytoplasmic sperm injection- in vitro fertilization” in the blue cluster. It is possible to understand this from the thickness of the line between them.

Keywords Trend Analysis

The upper graph in Figure 6 shows the change in the amount of usage of 10 keywords in time, and the lower



Figure 4. Word cloud and number of repetitions of keywords in the ICSI research area

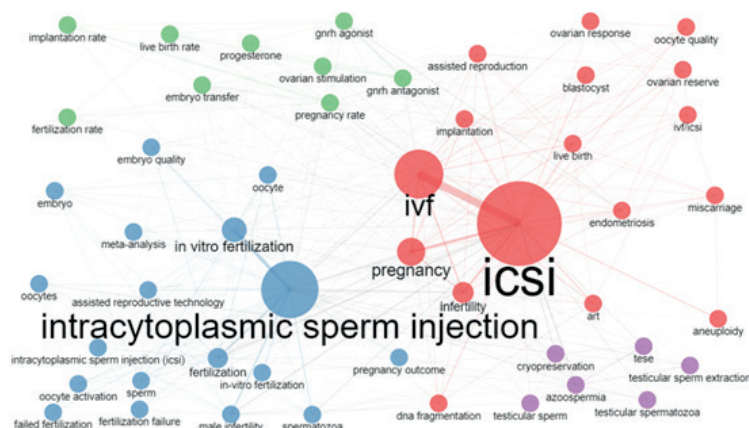


Figure 5. Co-occurrence network

graph shows the years in which the keywords are frequently used.

The alteration and trend of author keywords in time is presented in Figure 6. In order to analyze the ICSI issue in different time periods, The 29-year time interval starting from 1993 until 2021 is divided into ten time periods in which the first time period is 2 years and the following ones are 3 years. The first ten keywords of the authors were examined. The amount of use of all keywords has increased from 1993 to 2021. While the word ICSI was used once in 1993-1994, it was used 2468 times between 2019-2021. Along with the word “Intracytoplasmic sperm injection”, the author keywords “ICSI” and “Ivf” have been increasingly used.

While intracytoplasmic injection, subzonal insemination and spermatozoon keywords in the field of ICSI were more frequently used between 1993-1995, cumulative live birth rate, perinatal outcomes, cumulative live birth ve predictions keywords are more common nowadays.

The keyword ICSI (858), Intracytoplasmic sperm injection (516) and Ivf (390) have reached their highest use in 2017, 2002 and 2010, respectively.

Thematic Development Analysis

Strategic diagrams of the ICSI study topic are presented in Figure 7.

“Motor Themes”, is the first quarter theme. It forms the upper right part. Only one cluster was formed in the 2017-2021 period. “Embryo transfer” represented this cluster.

“Highly Developed and Isolated Themes”, is the second quarter theme. It forms the upper left part. Between the 2017-2021 period, “pregnancy outcome”, “fertilization failure” and “frozen-thawed embryo transfer” keywords represented the first, second and third clusters.

“Emerging or Declining Themes”, is the third quarter theme. It forms the lower left part. Between 2017-2021, “male infertility” keyword represented the first cluster.

“Basic and Transversal Themes”, is the fourth quarter theme. It forms the lower right part. Between 2017-2021, “iscsi”, “intracytoplasmic sperm injection” and “live birth” keywords represented the first, second and third clusters.

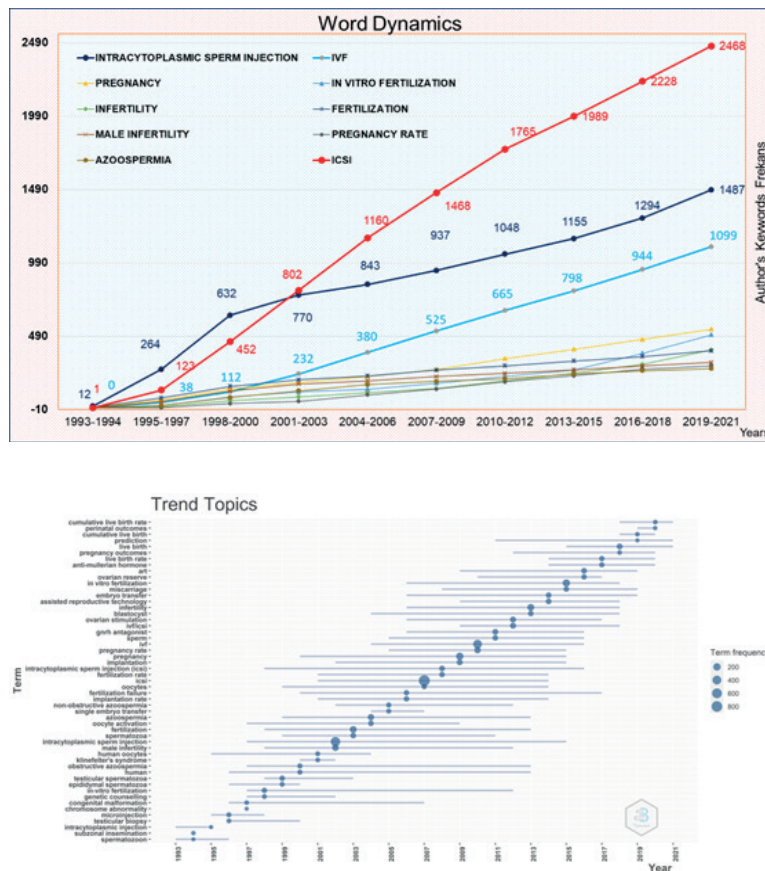


Figure 6. Change and orientation of keywords in the ICSI field according to the keyword frequency

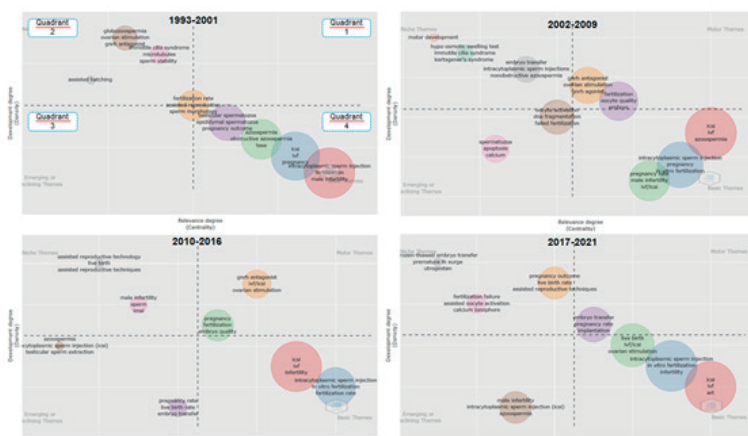


Figure 7. Strategic diagram of ICSI studies (1993–2021)

The four-period thematic evolution mapping, presented in Figure 8, was performed in addition to the four-period Thematic Mapping, in order to evaluate the development and change of ICSI themes over the years.

The principles in Figure 7 were used while creating the Thematic Evolution Map in Bibliometrix. When the diagram is examined, there are 8 themes in the first, third and fourth periods and 9 themes in the second period. The width of the node is proportional to the size of the linked keywords. The biggest theme in the 2017-2021 period was the word “intracytoplasmic sperm injection”. This word has been preserved as a theme for four periods. In addition, the word “icsi”, which is our other analysis word, remained as a theme for four periods. The themes of “live birth, icsi, male infertility, embryo transfer, pregnancy outcome, fertilization failure, frozen-thawed embryo transfer” along with the theme of “Intracytoplasmic sperm injection” are last period themes. While the recent term “intracytoplasmic sperm injection” is fed by the sub-period themes of “gnrh antagonist, male infertility, icsi, azoospermia”, it was fed by the themes of “ics, pregnancy rate” between 2010-2016.

In addition to the “Intracytoplasmic sperm injection” and “ICSI” themes; “assisted hatching, globozoospermia”, “oocyte activation, hypo-osmotic swelling test”, “gnrh antagonist, male infertility”, and “live birth, male infertility” themes were effective during 1993-2001, 2002-2009, 2010-2016 and 2017-2021. It was observed that different themes emerged as additional themes in 4 periods regarding our main study subject.

Citation Analysis

20 most cited articles about ICSI are listed according to their local citation (LC) numbers in Table 4. The article “Vansteirteghem AC, 1993, Hum Reprod” has reached 328 local citations and 1036 general citations, making it the most effective article on ICSI. The most cited articles in recent years are “Bonduelle M, 2002, Hum Reprod-a” and “Bonduelle M, 2002, Hum Reprod” which were published in 2002 and reached 69 local citations.

Annual Local Citations (LC/YYP) and Annual Global Citations (GC/YYP) are used to eliminate the disadvantage due to the limited citation time of the articles published in recent years. The article with the

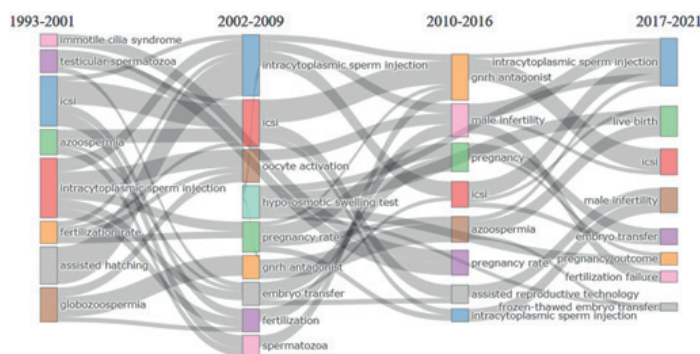


Figure 8. Thematic development of ICSI studies (1993–2021)

Table 4. 20 Most Cited Local Articles in the Field of ICSI

Document	YP	LC	LC/YYP %	GC	GC/YYP %	LC/GC Ratio %
Vansteirteghem AC, 1993, Hum Reprod	1993	328	11,31	1036	35,72	31,66
Vansteirteghem AC, 1993, Hum Reprod-a	1993	168	5,79	473	16,31	35,52
Nagy ZP, 1995, Hum Reprod-a	1995	117	4,33	355	13,15	32,96
Palermo G, 1993, Fertil Steril	1993	114	3,93	298	10,28	38,26
Silber SJ, 1995, Hum Reprod	1995	98	3,63	347	12,85	28,24
Tournaye H, 1994, Fertil Steril	1994	85	3,04	265	9,46	32,08
Nagy Z, 1995, Fertil Steril	1995	84	3,11	237	8,78	35,44
Bonduelle M, 2002, Hum Reprod-a	2002	73	3,65	364	18,20	20,05
Devroey P, 1995, Hum Reprod	1995	70	2,59	429	15,89	16,32
Bonduelle M, 2002, Hum Reprod	2002	69	3,45	301	15,05	22,92
Silber SJ, 1994, Hum Reprod	1994	68	2,43	272	9,71	25,00
Palermo GD, 1995, Fertil Steril	1995	67	2,48	268	9,93	25,00
Palermo GD, 1996, Hum Reprod	1996	66	2,54	111	4,27	59,46
Palermo GD, 1996, Hum Reprod-a	1996	66	2,54	90	3,46	73,33
Tesarik J, 1994, Hum Reprod	1994	65	2,32	274	9,79	23,72
Wennerholm UB, 2000, Hum Reprod	2000	57	2,59	257	11,68	22,18
Nagy ZP, 1994, Hum Reprod	1994	54	1,93	147	5,25	36,73
Liu J, 1995, Hum Reprod	1995	53	1,96	131	4,85	40,46
Palermo GD, 1999, Hum Reprod	1999	50	2,17	208	9,04	24,04
Bonduelle M, 1996, Hum Reprod-a	1996	49	1,88	130	5,00	37,69

Year of Publication (YP), Local Citations (LC), YYP= Year 2022-Year of Publication, Global Citations (GC)

highest LC/YYP (11.31) and GC/YYP (35.72) values is “Vansteirteghem AC, 1993, Hum Reprod”.

Another concept developed for the most cited articles is Local Citation Percentage (LC/GC Ratio %). The most influential article is “Palermo GD, 1996, Hum Reprod-a” with a value of 73.33% according to the percentage of Local Citations.

When citation analyzes are examined, it is possible to say that “Vansteirteghem AC, 1993, Hum Reprod” article titled “High fertilization and implantation rates after intracytoplasmic sperm injection” is the most influential article in the ICSI field of study (33).

Collaboration Analysis

The countries that cooperate internationally about the study field of ICSI and the amount of cooperation are shown in Figure 9. Countries marked in dark blue in the figure are those that produced more articles. It is seen that the countries marked with dark blue are European countries, USA, China, Turkey, Egypt, Australia, Brazil, Iran. The thickness of the line indicates the amount of international cooperation.

As seen in Figure 9, the most international cooperation was from Italy to Spain (20). The second most international cooperation was between Holland and Belgium (18). It is seen that many countries in Europe both produce sufficient articles and have good cooperation between countries.

Studies have shown that; collaboration between research centers is crucial to address and solve complex problems in the real world (34).

DISCUSSION

ICSI is the most widely used assisted reproductive technology method today and is used in 66.5% fertility centers (35). This study aimed to determine the inclusive structure of articles about ICSI, the evolution of research themes, the research tendencies and their geographical distribution. Bibliometric science mapping was used for this purpose. Within the scope of the research, the WoS database was examined and a total number of 2379 articles, matching the search criteria, were analyzed.

It has been determined that the first article on ICSI was published in 1993, there was a serious increase



Figure 9. Collaboration world map

in the number of articles until 1998, and it was mostly produced in 2021. The widespread use of the ICSI method and the need to clarify its results and the cost-effectiveness balance (36) are considered to be effective in the increase in the number of academic studies on this subject.

USA, China, Belgium, Turkey and Italy are among the leading countries when countries are evaluated according to the number of articles published about ICSI. The USA ranked first in the number of single-country, multi-country and total publications. While the use of ICSI in cases with male factor infertility in the USA increased from 76.3% to 93.3% between 1996-2012, ICSI use in non- male factor infertility increased from 15.4% in 1996 to 66.9% in 2012 (5). It is thought that the increasing demand for ICSI in the USA is also reflected on the researches and plays a role with the USA as the country with the most publications. In our research, it was found that the country with the highest MCP ratio, which is defined as the division of multi-country publications by the total number of publications, is Greece. In terms of cooperation between countries, it is seen that the highest rate of joint publication is between academics of Italian-Spain and Dutch-Belgian origin. In a study examining the use of ICSI according to countries, it was seen that Italy, Belgium, Netherlands, Germany, Spain and Greece use this method most common in Europe (37). It can be said that Countries' ICSI use is parallel to the publishing and cooperation between countries.

When an evaluation is made in terms of the authors, it is seen that Paul Devroey, who is working at the Center for Reproductive Medicine, Free University of Brussels, Belgium, ranks first with 101 publications and 10471 citations. Prof. Dr. Herman Tournaye, who is the head of the department at the Centre for Reproductive Medicine, Vrije Universiteit Brussel, Brussels, Belgium, ranks second with 76 publications and 5702 citations. On the other hand, Prof. Dr. André C Van Steirteghem, who is working at Centre for Reproductive Medicine, Vrije

Universiteit Brussel, Brussels, Belgium, ranks third with 46 publications and 3662 citations. Prof. Dr. Petra de Sutter, who was working at Department of Reproductive Medicine, University of Ghent, Belgium, ranks fourth with 27 publications and 1244 total citations. Although Sutter's first publication in this field was a few years ago (2018), she is a remarkable researcher in terms of publications and citations. It is seen that the most influential writers in the field of ICSI are from Belgium.

When an evaluation is made in terms of the journals, "Human Reproduction", which received 38665 citations with a total of 615 articles on ICSI, the first of which was in 1993, is the most influential journal in this field in terms of citations and indexes. This journal, which publishes reproductive studies, is the official journal of the European Society of Human Reproduction and Embryology. "Fertility and Sterility", which is the official journal of the American Society for Reproductive Medicine, has received 19514 citations with a total of 417 articles, the first of which was in 1993, and is the second most influential journal on this subject. "Reproductive Biomedicine Online" journal, which is the official publication of Mediterranean Society for Reproductive Medicine, Canadian Fertility & Andrology Society, Academy of Clinical Embryologists and Controversies in Obstetrics, Gynecology and Infertility societies, is the third most influential journal about the field of ICSI with a total of 192 publications and 5677 citations, the first of which was in 2004. It is thought that the high impact factors of journals and being official publication of professional societies have been influential in their leading position in this field. It is possible to say that the "International Journal of Fertility & Sterility" published by the Royan Institute/Iran has quickly become influential and attracted attention in the field of research with 24 publications and 184 citations, the first of which was in 2008.

The most frequently used keyword in ICSI is the word "Intracytoplasmic sperm injection" and its abbreviation "ICSI", as expected. "IVF", "Pregnancy" and "Infertility"

are the other most frequently used keywords. Infertility affects 7.5 million women in the United States and one in eight couples have trouble about becoming pregnant or maintaining a pregnancy (38). Both the use of these services and the number of fertility clinics that offer these services have steadily increased in the USA since the first baby conceived with assisted reproductive technology was born in 1981. IVF, an assisted reproductive technology, is a successful treatment method for infertility. IVF involves ovarian stimulation with gonadotropin hormones followed by retrieval of oocytes under sedation followed by fertilization by sperm in the laboratory and developing embryos in culture before transfer to the uterus (39,40). Since ICSI is a method used to achieve pregnancy, especially in male factor infertility and in cases where traditional IVF is not successful, it is perfectly normal to use it with these related keywords.

When the citation analysis is examined, the study named “High fertilization and implantation rates after intracytoplasmic sperm injection” published in the Human Reproduction journal in 1993 by André C Van Steirteghem et al., is the most cited study in this field with 328 local and 1036 general citations. In this study, 150 infertile couples, who failed to fertilize oocytes after standard IVF procedures or were not admitted to IVF because there was not enough motile sperm in the ejaculate underwent ICSI in 150 consecutive treatment cycles and high pregnancy rates were determined as a result of the study (33). Similarly, the study named “Higher success rate by intracytoplasmic sperm injection than by subzonal insemination. Report of a second series of 300 consecutive treatment cycles” published in the Human Reproduction journal in 1993 by André C Van Steirteghem et al., is the second most influential study with 167 local and 473 general citations. In this study, Subzonal insemination (SUZI) and ICSI were performed over 300 treatment cycles in couples unable to be assisted by conventional IVF. It was found that more oocytes were damaged in ICSI (13.5%) than SUZI (7.1%), the normal fertilization rate was significantly higher in ICSI (51.0%) than SUZI (14.3%) and was associated with semen features (41). The study named “The result of intracytoplasmic sperm injection is not related to any of the three basic sperm parameters” published in the Human Reproduction journal in 1995 by Nagy et al., is the third most influential study with 168 local and 473 general citations. The relationship between three basic sperm parameters (total sperm count, sperm motility and morphology) and ICSI result was analyzed retrospectively in this study in terms of fertilization, embryo development and pregnancy rates. The results showed that neither the type nor the degree of sperm disorder had a significant effect on the outcome of ICSI (42).

It is evaluated that this research is original and will contribute to science in terms of research subject, ICSI, and science mapping

REFERENCES

1. Devroey P, Van Steirteghem A. A review of ten years experience of ICSI. Hum Reprod Update. 2004;10:19–28.
2. Esteves SC. Intracytoplasmic sperm injection versus conventional IVF. Lancet. 2021;397(10284):1521–1523.
3. Palermo G, Joris H, Devroey P, Van Steirteghem AC. Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. Lancet. 1992;340:17–18.
4. O'Neill CL, Chow S, Rosenwaks Z, Palermo GD. Development of ICSI. Reproduction. 2018;156(1):F51–F58.
5. Boulet SL, Mehta A, Kissin DM, Warner L, Kawwass JF, Jamieson DJ. Trends in use of and reproductive outcomes associated with intracytoplasmic sperm injection. JAMA. 2015;313(3):255–263.
6. Ch De Geyter, C Calhaz-Jorge, MS Kupka, C Wyns, E Mocanu, T Motrenko, et al, The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE), ART in Europe, 2014: results generated from European registries by ESHRE: The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE), Hum Reprod. 2018;33(9): 1586–1601
7. Esteves SC, Roque M, Bedoschi G, Haahr T, Humaidan P. Intracytoplasmic sperm injection for male infertility and consequences for offspring. Nat Rev Urol. 2018; 15: 535–562.
8. de Mouzon J, Chambers GM, Zegers-Hochschild F, Mansour R, Ishihara O, Banker M, et al. International committee for monitoring assisted reproductive technologies world report: assisted reproductive technology 2012. Hum Reprod. 2020; 35(8): 1900–1913.
9. Johnson LN, Sasson IE, Sammel MD, Dokras A. Does intracytoplasmic sperm injection improve the fertilization rate and decrease the total fertilization failure rate in couples with well-defined unexplained infertility? A systematic review and meta-analysis. Fertil Steril. 2013;100(3):704–711.
10. Foong SC, Fleetham JA, O'Keane JA, Scott SG, Tough SC, Greene CA. A prospective randomized trial of conventional in vitro fertilization versus intracytoplasmic sperm injection in unexplained infertility. J Assist Reprod Genet. 2006;23(3):137–140.
11. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Intracytoplasmic sperm injection (ICSI) for non-male factor indications: a committee opinion. Fertil Steril. 2020;114(2):239–245.
12. Esteves SC, Yarali H, Vuong LN, Carvalho JF, Ozbek IY, Polat M, et al. Low prognosis by the POSEIDON criteria in women undergoing assisted reproductive technology: a multicenter and multinational prevalence study of over 13000 patients. Front Endocrinol (Lausanne). 2021; 12: 630550.
13. Tararbit K, Lelong N, Thieulin AC, Houyel L, Bonnet D, Goffinet F, et al. The risk for four specific congenital heart defects associated with assisted reproductive techniques: a population-based evaluation. Hum Reprod. 2013;28:367–374.
14. Stern JE, Nangia AK. When do we use intracytoplasmic sperm injection? Fertil Steril. 2020;114(4):746–747.
15. Franasiak JM, Polyzos NP, Neves AR, Yovich JL, Ho TM, Vuong LN, et al. Intracytoplasmic sperm injection for all or for a few? Fertil Steril. 2022;117(2):270–284.
16. Baysal YE. Pediatric nephrotic syndrome with science mapping method. J Soc Anal Health. 2022;2(2):62–67.
17. Kurutkan MN, Orhan F. Kalite Prensipierinin Görsel Haritalama Tekniğine Göre Bibliyometrik Analizi. Ankara: SAGE Publications Ltd., 2018.
18. Chen C. Science mapping: A systematic review of the literature. J Data Inf Sci. 2017;2(2):1–40.
19. Andersen N, Swami V. Science mapping research on body image: A bibliometric review of publications in Body Image, 2004–2020. Body Image. 2021;38:106–119.

20. Ma X, Zhang L, Wang J, Luo Y. Knowledge domain and emerging trends on echinococcosis research: a scientometric analysis. *Int J Environ Res.* 2019;16 (5). 842.
21. Aria M, Cuccurullo C. Bibliometrix: An R-tool for comprehensive science mapping analysis. *J Informetr.* 2017;11:959–975.
22. Kamdem JP, Duarte AE, Lima KRR, Rocha JBT, Hassan W, Barros LM, et al. Research trends in food chemistry: A bibliometric review of its 40 years anniversary (1976–2016). *Food Chem.* 2019;294:448–457.
23. Egghe L. Theory and practice of the g-index. *Scientometrics.* 2006;69(1):131–152.
24. Nowak JK, Lubarski K, Kowalik LM, Walkowiak J. H-index in medicine is driven by original research. *Croat Med J.* 2018;59(1):25–32.
25. Orimoloye IR, Ololade OO. Potential implications of gold-mining activities on some environmental components: a global assessment (1990 to 2018). *J King Saud Univ.* 2020;32(4):2432–2438.
26. Zheng X, Le Y, Chan APC, Hu Y, Li Y. Review of the application of social network analysis (SNA) in construction project management research. *Int J Proj Manag.* 2016;34:1214–1225.
27. Callon M, Courtial JP, Laville F. Co-word analysis as a tool for describing the network of interactions between basic and technological research: The case of polymer chemistry. *Scientometrics.* 1991;22(1):155–205.
28. Schögl J-P, Stumpf L, Baumgartner RJ. The narrative of sustainability and circular economy-A longitudinal review of two decades of research. *Resour Conserv Recycl.* 2020;163:105073.
29. Nasir A, Shaukat K, Hameed IA, Luo S, Alam TM, Iqbal F. A bibliometric analysis of corona pandemic in social sciences: A review of influential aspects and conceptual structure. *IEEE Access.* 2020;8:133377–133402.
30. Cobo MJ, López-Herrera AG, Herrera-Viedma E, Herrera F. Science mapping software tools: Review, analysis, and cooperative study among tools. *J Am Soc Inf Sci Technol.* 2011;62(7):1382–1402.
31. Schmidt M. The sankey diagram in energy and material flow management. *J Ind Ecol.* 2008;12:82–94.
32. Yao Q, Chen K, Yao L, Lyu P, Yang T, Luo F, et al. Scientometric trends and knowledge maps of global health systems research. *Health Res Policy Syst.* 2014;12:26.
33. Van Steirteghem AC, Nagy Z, Joris H, Liu J, Staessen C, Smitz J, et al. High fertilization and implantation rates after intracytoplasmic sperm injection. *Hum Reprod.* 1993;8(7):1061–1066.
34. Secinaro S, Calandra D, Petricean D, Chmet F. Social finance and banking research as a driver for sustainable development: A bibliometric analysis. *Sustainability.* 2021;13(1): 330.
35. Haddad M, Stewart J, Xie P, Cheung S, Trout A, Keating D, et al. Thoughts on the popularity of ICSI. *J Assist Reprod Genet.* 2021;38(1):101–123.
36. Bosch E, Espinós JJ, Fabregues F, Fontes J, García-Velasco J, Llácer J, et al. Spanish infertility SWOT group (SISG). Always ICSI? A SWOT analysis. *J Assist Reprod Genet.* 2020;37(9):2081–2092.
37. Nyboe Andersen A, Carlsen E, Loft A. Trends in the use of intracytoplasmic sperm injection marked variability between countries. *Hum Reprod Update.* 2008;14(6):593–604.
38. Sunderam S, Kissin DM, Crawford SB, Suzanne GF, Denise JJ, Warner L, et al. Assisted reproductive technology surveillance – United States, 2013. *MMWR Surveill Summ.* 2015; 64(11):1–25.
39. Sullivan-Pyke CS, Senapati S, Mainigi MA, Barnhart KT. In Vitro fertilization and adverse obstetric and perinatal outcomes. *Semin Perinatol.* 2017;41(6):345–353.
40. Sunderam S, Kissin DM, Crawford SB, Folger SG, Boulet SL, Warner L, et al. Assisted reproductive technology surveillance – United States, 2015. *MMWR Surveill Summ.* 2018;67(3):1–28.
41. Van Steirteghem AC, Liu J, Joris H, Nagy Z, Janssenswillen C, Tournaye H, et al. Higher success rate by intracytoplasmic sperm injection than by subzonal insemination. Report of a second series of 300 consecutive treatment cycles. *Hum Reprod.* 1993;8(7):1055–1060.
42. Nagy ZP, Liu J, Joris H, Verheyen G, Tournaye H, Camus M, et al. The result of intracytoplasmic sperm injection is not related to any of the three basic sperm parameters. *Hum Reprod.* 1995;10(5):1123–1129.