



Recurrent Pregnancy Loss: A Bibliometric Review

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Abstract

Background: The research combined different bibliometric techniques to analyze systematically recurrent pregnancy loss (RPL) documents from 1970 to 2023.

Methods: Overall, 1287 documents from the Web of Science database associated with recurrent pregnancy loss between 1970 and 2023 were identified for more than 300 journals. The data were analyzed with VOSviewer software.

Results: The trend of paying attention to the topic of RPL can be divided into three periods. The number of publications on RPL increased significantly after 2010. Most of the papers were published in Obstetrics and Gynecology and Reproductive Biology areas. Utilizing co-occurrence and co-citation analysis, our study found that the most influential documents mapped the knowledge structure, and projected future research directions. The co-occurrence analysis showed five clusters even though the co-citation analysis designates four.

Conclusion: RPL has increased in recent years exponentially and some areas were explained carefully, therefore these results could be used as a research agenda for the future direction by a range of interested beneficiaries.

Keywords: Recurrent pregnancy loss; Bibliometric; Co-occurrence; Co-citation; Web of science database

Introduction

Recurrent pregnancy loss (RPL) is a public, yet indefinable, problem of pregnancy (1). RPL is defined as two or more pregnancy losses, including embryonic and fetal loss before gestational weeks 20–24 (2), which bring about important economic and psychological concerns in society (3).

RPL is experienced in 2%-5% of the Obstetric population (4,5), and in 50% the reasons are unknown therefore RPL is a puzzling state for Obstetricians to manage such patients (4). More than half of RPL remains unexplained (6). Since the 21st century, important improvement has been made in the area of RPL, increasing the number

of published documents in the RPL area. Bibliometrics uses different techniques to study publications, especially those in the scientific lines (7,8).

Based on the current knowledge, no bibliometric study was conducted on RPL. This study has filled an important research gap using bibliometric review, a general domain analysis and visualization process, and bibliometric citation and co-citation. Our findings will help future investigators recognize the etiology and risk factors related to the RPL area. It will also improve the depth and develop the body of knowledge RPL area by looking at the bibliometric data of 1287



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documents from 387 journals from 1970 to 2023. Web of Science (WoS), is well-thought-out one of the broadest databases for bibliometrics and was used for data retrieval (9,10). Therefore, this study aimed to address the following questions: What are the overall trends in RPL research? Who are the leading countries, authors, and journals in the RPL area? What are the global associations and important networks among the different nations and countries based on the citation report?

Methods

This study used the bibliometric method as a main research method to study the structure and foundation of the RPL field (11). This study first recognized databases and defined which best met the study's requirements. Qualified documents were collected from the WOS database from 1970 to July 2023. This survey limited the initial search to documents that encompassed "recurrent pregnancy loss*" or "missed-abortion*" or "missed abortion*" in the "TITLE". In the initial investigation, 2719 papers were explored. Finally, the search strategy was restricted to 'article' and "English" language. The review of the literature displayed that there were 1289 documents (h-index 72, average citations per item 20.28, sum of times cited 26135) around RPL printed from 1970 to 2023.

Of these publications, 598 were in Obstetrics Gynecology, 463 in Reproductive Biology, 194 in Immunology, 120 in Genetics Heredity, 105 in Medicine General Internal, 59 in Biochemistry Molecular Biology, 59 in Medicine Research Experimental, 49 in Endocrinology Metabolism, 37 in Cell Biology, 34 in Hematology, 31 in Developmental Biology, and 31 in Multidisciplinary Sciences area. VOSviewer software was used for data analysis (12).

Results

Distribution of RPL documents per year

Fig. 1 shows the graph of the number of documents plus the number of citations from 1970 to

2023 in the field of RPL. The general trend follows exponential growth ($y=5.2054e0.122x$, $R^2=0.94$). In addition, due to the number of documents and the exponential diagram of citations, significant results are obtained. Moreover, the trend of paying attention to the topic of the RPL can be divided into three timespans. During the first era of 1970-1990, the total number of published documents by the end of 1990 was less than 60 documents and accounted for only 4% of the total publications. The RPL has not received much attention in this period. The second phase, from 1991 to 2010, saw a steady upward trend in the number of publications and citations. Since 2011, the growth of documents and citations in this field has been increasing, so 74% of the total articles are dedicated to this period. Overall, 1287 documents were involved. The growth in RPL research between 1970 and 2023 based on publications (TS) and the number of citations (TC) each year was revealed in Fig. 1. About 75% of documents were published after the 2010 year. Most of the documents were published in 2022, 2021, and 2020; fewer were in the 70s.

Most Authors, Countries, Organizations, and Journals in the RPL discipline

Authors

The top 10 document-producing authors, nations/regions, and organizations are documented. About 8000 authors contribute to this area. The ranked authors who reproduced RPL documents from 1970 to 2023 were Kwak-Kim, Joanne; Sugiura-Ogasawara, Mayumi; Kim, and Nam Keun.

Countries

About 89 countries and regions contributed to this area. The top 10 nations in the RPL area of research were selected. The "United States" is the first dominant country (TS = 235), and after that "Peoples R China" (TS = 214) and Iran (TS=100). Japan (TS = 93); Turkey (TS = 75); and India (TS = 67) were at the next positions.

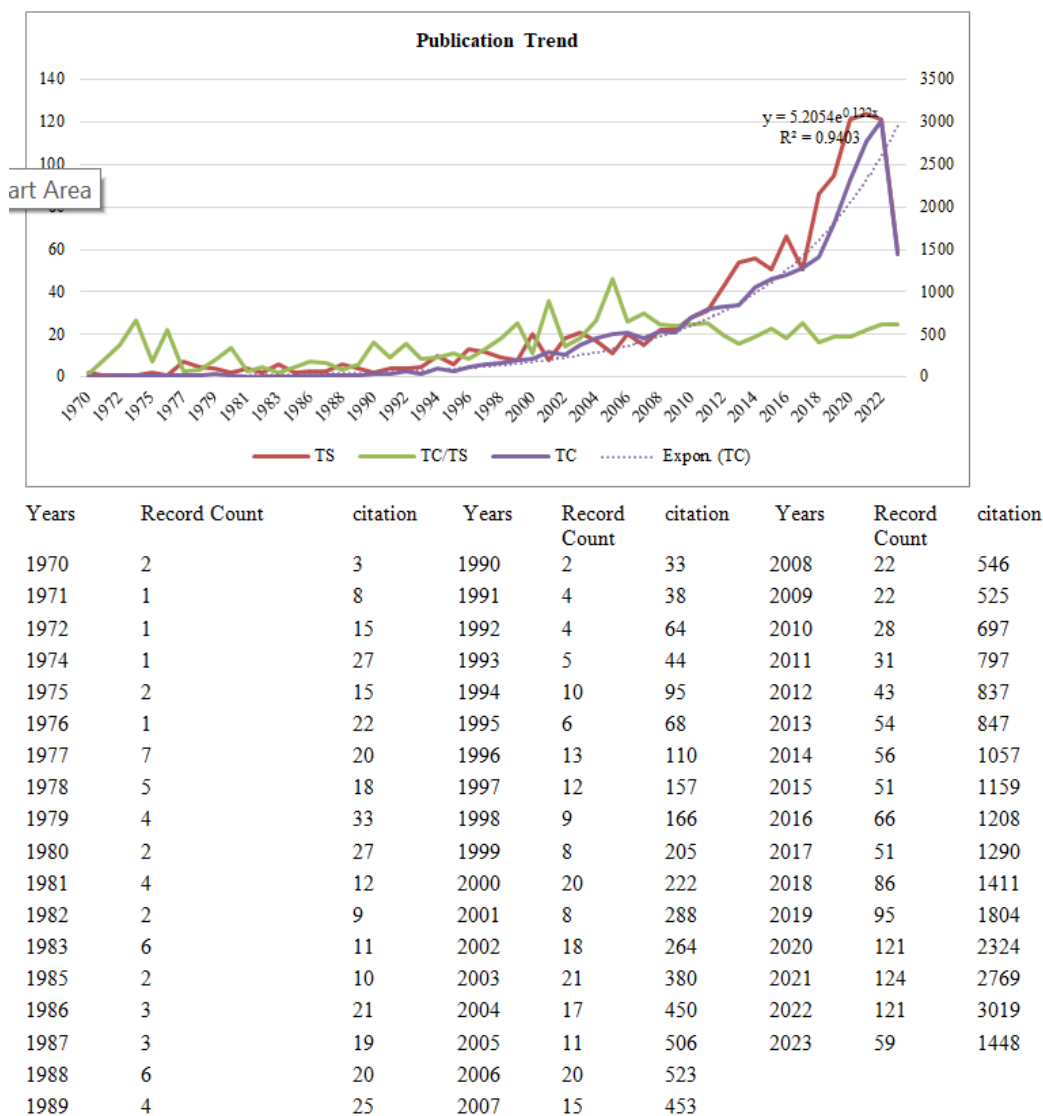


Fig. 1: Number of publications and citations per year (1970 – 2023)

Organizations

The research comprised 1600 organizations and universities from different geographical regions. The top 10 organizations involved Rosalind Franklin Univ Med & Sci (TS = 33); Cha Univ (TS = 25); Islamic Azad Univ (TS = 24); and Shanghai Jiao Tong Univ (TS = 24).

Journals

American Journal of Reproductive Immunology (TS=95); Fertility and Sterility (TS=74); Journal of Reproductive Immunology (TS=49); Human

Reproduction (TS=42); Journal of Assisted Reproduction and Genetics (TS=40); and Journal of Obstetrics and Gynaecology Research (TS=31) were the top journals published RPL (Fig. 2). The source production over time found that the American Journal of Reproductive Immunology and the European Journal of Obstetrics & Gynecology and Reproductive Biology were the journals that in recent years published RPL (Fig. 3).

Highly-Cited publications

About 30% of the most-cited articles were published in Fertility and Sterility. “Evaluation and

treatment of RPL” is the most cited document published in Fertility and Sterility (TC=620) (13). Antiphospholipid antibody-associated RPL (14), ESHRE guideline (15), and definitions of infertility and RPL (16) were at the next stages (Tables 1, 2). Most of these highly-cited documents were published in Fertility and Sterility. In sum, these

most cited documents showed some main characteristics of the RPL, such as the etiology of RPL (17), definitions (16,18, 19), treatment (20), the role of enoxaparin (21), hypercoagulable state mutation (22), antithyroid antibodies (23), antiphospholipid antibody (14, 24), and gestational outcome (25) in RPL.

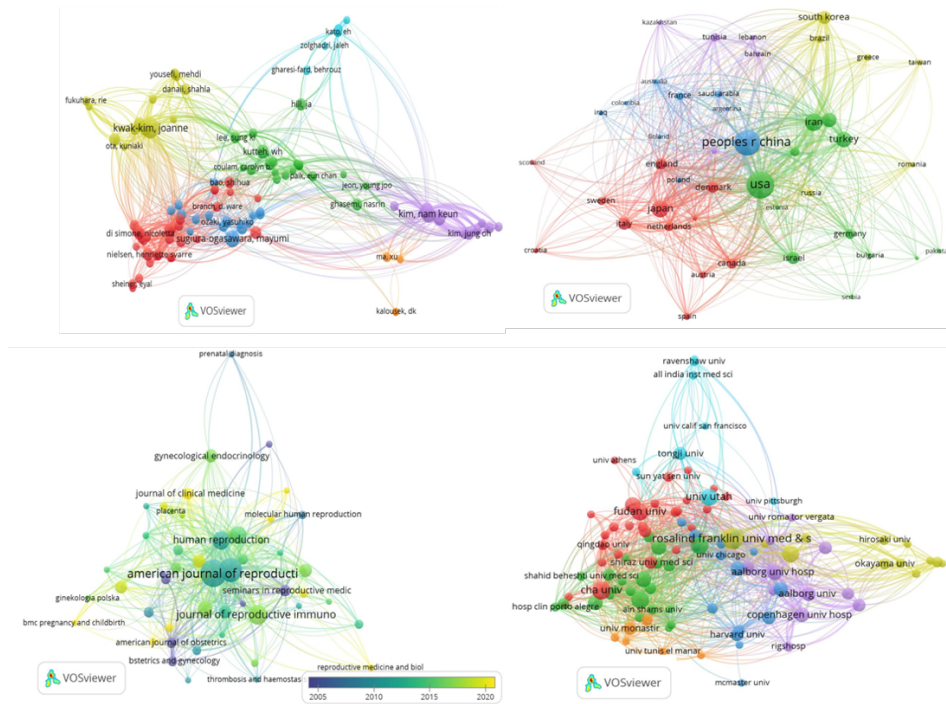


Fig. 2: The citation map of Authors, Countries, Journals, and Organizations (A, B, C, D)

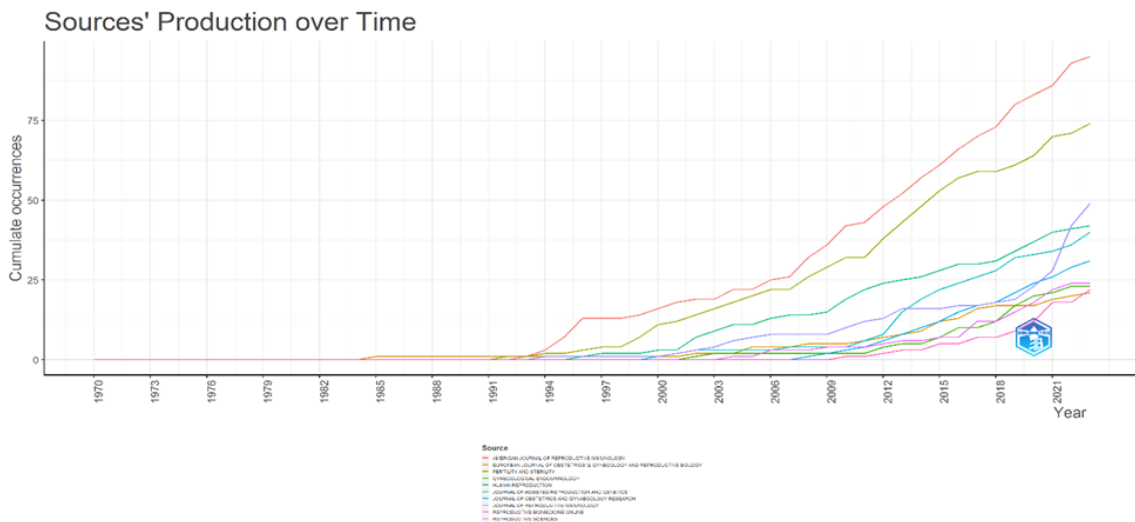


Fig. 3: Source production over time

Table 1: The most cited Authors, Countries, Organizations, and Journals in the RPL areas

Country	cluster	TS	TC	Author	cluster	TS	TC	Organization	cluster	TS	TC	Journal	cluster	TS	TC
USA	2	235	10027	Kwak-Kim, Joanne	4	29	679	Rosalind Franklin Univ Med & Sci	4	33	839	American Journal of Reproductive Immunology	3	95	2749
Peoples R China	3	214	2119	Sugiura-Ogasawara, Mayumi	3	19	284	Cha Univ	1	25	402	Fertility and Sterility	4	74	4285
Iran	2	100	1004	Kim, Nam Keun	5	18	220	Islamic Azad Univ	2	24	221	Journal of Reproductive Immunology	5	49	686
Japan	1	93	2028	Lee, Woo Sik	5	16	191	Shanghai Jiao Tong Univ	2	24	315	Human Reproduction	6	42	2176
Turkey	2	75	731	Kim, Ji Hyang	5	15	191	Nagoya City Univ	4	22	343	Journal of Assisted Reproduction and Genetics	2	40	567
India	2	67	815	Kutteh, Wh	2	14	1598	Fudan Univ	1	21	208	Journal of Obstetrics and Gynaecology Research	1	31	324
South Korea	4	56	1012	Gilman-Sachs, Alice	4	13	426	Univ Utah	6	21	970	Reproductive Biomedicine Online	2	24	392
Italy	1	48	570	Christiansen, Ole Bjame	1	12	495	Aalborg Univ Hosp	5	19	528	Gynecological Endocrinology	6	23	120
Occupied Palestine	2	47	1198	Kim, Jung Oh	5	12	124	Shandong Univ	1	19	184	Reproductive Sciences	5	22	145
Denmark	1	41	944	Kim, Young Ran	5	12	105	Tabriz Univ Med Sci	2	18	266	European Journal of Obstetrics & Gynecology and Reproductive Biology	1	21	215

A three-field plot: the Sankey diagram

In this study, the Sankey diagram was used to evaluate the “flow” among the country, journals, and keywords. The results picture the interconnections in RPL areas between 1970 and 2023. As shown in Fig. 4, the three-field plot exemplifies the flow trend between two or more journals

and countries. China is working with most of the top affiliations regarding topics connected to RPL and missed abortion. Besides, the other major suppliers, like Iran, USA, Korea, Japan, Italy, and India, have made important assistance according to published documents in the RPL area.

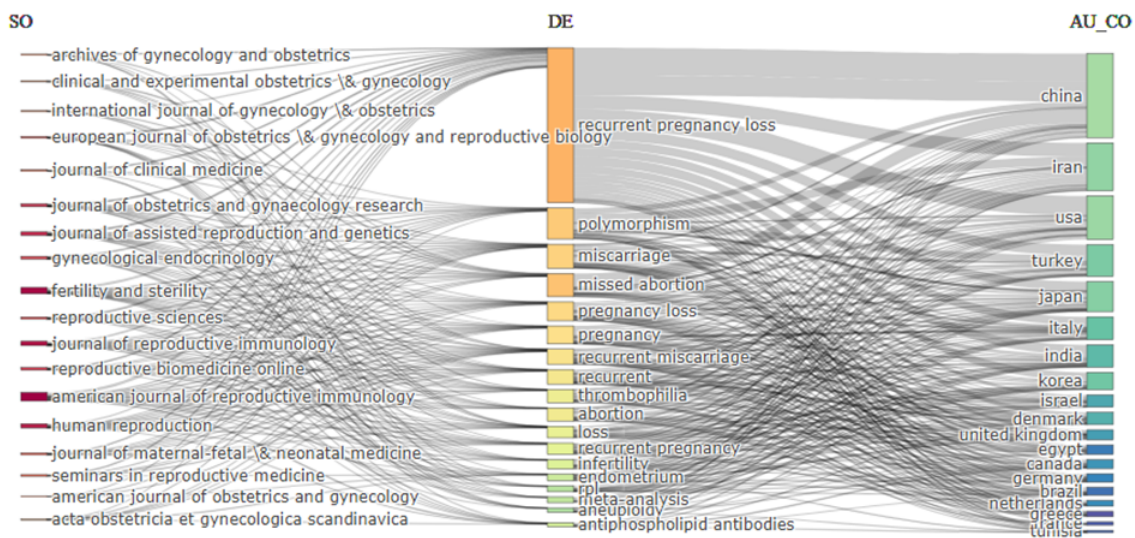


Fig. 4: A Sankey diagram

Table 2: Highly cited publications

<i>Title</i>	<i>Reference</i>	<i>Source Title</i>	<i>Year</i>	<i>TC</i>
Evaluation and treatment of recurrent pregnancy loss: A committee opinion	(13)	Fertility and Sterility	2012	620
Antiphospholipid antibody-associated recurrent pregnancy loss: Treatment with heparin and low-dose aspirin is superior to low-dose aspirin alone	(14)	American Journal of Obstetrics and Gynecology	1996	607
ESHRE guideline: recurrent pregnancy loss	(15)	Human Reproduction Open	2018	387
Definitions of infertility and recurrent pregnancy loss: A committee opinion	(16)	Fertility and Sterility	2013	324
Increased T helper 1 cytokine responses by circulating T cells are present in women with recurrent pregnancy losses and infertile women with multiple implantation failures after IVF	(26)	Human Reproduction	2003	314
Definitions of infertility and recurrent pregnancy loss	(18)	Fertility and Sterility	2008	294
Natural Selection of Human Embryos: Impaired Decidualization of Endometrium Disables Embryo-Maternal Interactions and Causes Recurrent Pregnancy Loss	(27)	PLOS One	2010	258
Sperm DNA fragmentation is increased in couples with unexplained recurrent pregnancy loss	(28)	Archives of Andrology	2003	246
Low Molecular Weight Heparin and Aspirin for Recurrent Pregnancy Loss: Results from the Randomized, Controlled HepASA Trial	(29)	Journal of Rheumatology	2009	243
The gestational outcome in thrombophilic women with recurrent pregnancy loss treated by enoxaparin	(25)	Thrombosis and Haemostasis	2000	241

Co-occurrence Analysis

Of the 4218 terms, 182 keywords occurred at least 10 times. The most applied topics published related to RPL are indicated in red, blue, green, and yellow colors. It can be observed from the Fig. 5 that the dominating keywords are recurrent pregnancy loss occurring at least 630 times, miscarriage 437 times, expression and spontaneous-

abortion with 187 times, risk 124 times, missed abortion 122 times and polymorphism 108 times related to 2, 5, 2, 3, 6, 5, and 6 clusters. Additionally, as Fig. 5b, depicts, yellow keywords specify the recent keywords that have appeared in recently published documents in recent years. These keywords are NK cells, implantation failure, depression, stress, autoimmunity, and abnormalities.

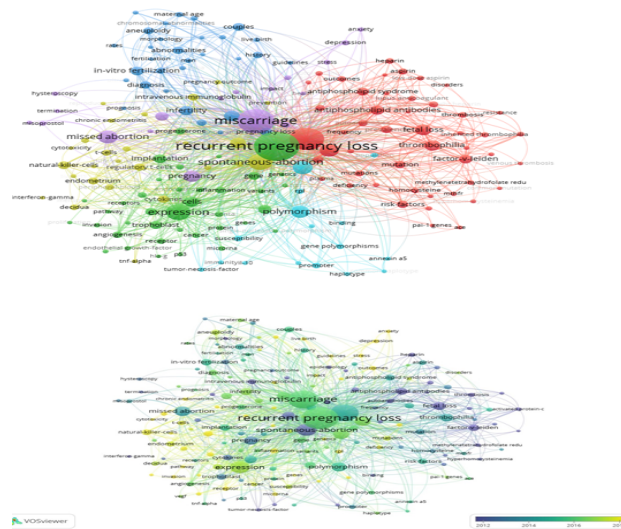


Fig. 5: Co-occurrence analysis of network visualization (a) and overlay visualization (b)

Co-citation Analysis

Co-citation analysis was used to create a forward-looking evaluation of the intellectual structure of the RPL. Four clusters have been found and each cluster is symbolized with a different color. The clusters could be examined further to know the main emphasis and theme of each. Cluster one (Red): The definition and foundation of the RPL (13,16,18,19,30-36) were the main areas of study

of the first cluster. Cluster two (Green): The etiology and outcomes of the RPL (37-43) were the main areas of study of the second cluster. Cluster three (Blue): Thrombophilic disorders (44-50) were the main area of study of the third cluster. Cluster four (Yellow): Antiphospholipid syndrome (51-54) was the main area of study of the fourth cluster (Fig. 6).

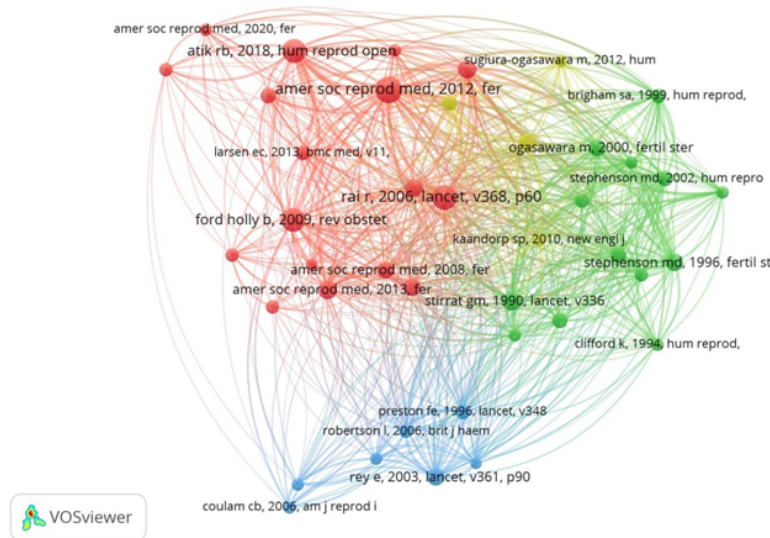


Fig. 6: The co-citation Map

Collaboration Analysis

The major association occurred between the USA and the people R China in first place, then the USA and South Korea, Japan, and Germany. It

can certainly be perceived that the USA is the first provider and collaborator in RPL. The Peoples R China, Iran, Japan, and Turkey were in the next stages (Fig. 7).

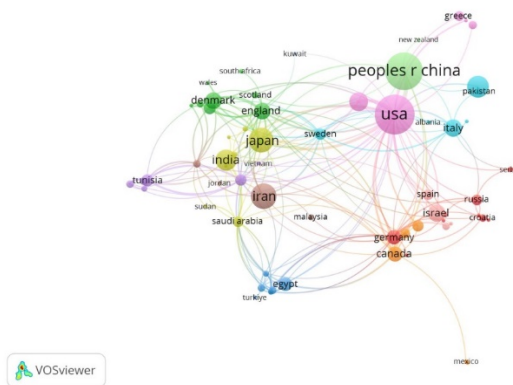


Fig. 7: Country Collaboration

Discussion

The RPL field is plentiful and derives from a variety of researchers from different backgrounds. This study aimed to assess 'RPL' trends between 1970 and 2023. This study suggests a regional imbalance in the generation of knowledge in the RPL area: the USA, the People's Republic of China, and Iran. However, a few documents were published in Africa and low-income countries. This national imbalance may be due to the differences in the incidence of RPL and the lack of researchers practitioners and hospitals that can diagnose and manage RPL. It is significant to remember that the source with high impact factors is inclined to have the highest counts of documents published about RPL. American Journal of Reproductive Immunology, Fertility and Sterility, and Journal of Reproductive Immunology are the leaders in publishing RPL documents. Nevertheless, journals have increased their production and influence in RPL because of the development of various research groups and collaborations around the world. This issue shows that researchers are more willing to publish in specialized journals than public journals.

The co-occurrence analysis found that RPL clusters mainly focused on keywords such as women, spontaneous abortion, risk, polymorphism, fetal loss, thrombophilia, and expression. Although, in only 50% of cases, the etiology of RPL was known, and the remaining 50% are considered unexplained and it appears that different factors play a key role (55,56).

Our result found that the subject of evaluation and treatment of RPL is the most cited document (13). Antiphospholipid antibody-associated RPL (14), ESHRE guideline (15), and definitions of infertility and RPL (16) were at the next stages. The issues such as treating and defining of the infertility are very important for researchers.

Several factors affect RPL such as congenital and anatomical causes, acquired defects, endocrine disorders such as hyperprolactinemia, polycystic ovary syndrome, insulin resistance, untreated diabetes, luteal phase defects in thyroid function,

thyroid antibodies, obesity, genetic factors, blood coagulation syndrome (55). The text-mining analysis found that the etiology of the RPL mainly consists of embryonic karyotype (51), antiphospholipid syndrome, uterine abnormalities, and abnormal chromosomes (57), (58), genetic, anatomical, and infectious factors, auto-immune system abnormalities and endocrine disorders (3), thrombophilia (4), male factors (3), parental chromosomal abnormalities, untreated hypothyroidism, uncontrolled diabetes mellitus, certain uterine anatomic abnormalities, and antiphospholipid antibody syndrome, endocrine disorders, heritable and acquired thrombophilia's, immunologic abnormalities, infections, and environmental factors (59). Pre-implantation genetic diagnosis significantly reduced spontaneous abortions (60). Enoxaparin (4, 25, 61), aspirin, and progesterone (4) are safe and effective in the prevention of RPL.

Limitation

We disclose the dramatic increase in global RPL literature; however, this study is not far from limitations. First, the WoS database was used only as a source of study and it was not possible to mix data from other databases. We encourage future researchers to integrate other databases such as PubMed, Scopus, and Google Scholar for evaluating the RPL literature. The second limitation of this study is a publication not written in English and was not article type (book chapter, proceeding paper, meeting abstract, letter, and editorial materials) were not selected, which helped with the bibliometric analysis. Finally, data reduction needs the definition of thresholds that ultimately change the results (62).

Conclusion

The presented study used bibliometric analysis methods to evaluate the 53-year history of the RPL field and determine the most influential documents, authors, journals, and nations. Our survey consisted of 1287 RPL documents pub-

lished in 387 journals. The first document around RPL was found in 1970, and since then, the number of publications in this field has been steadily increasing, reaching 1,287 articles published until June 2023. The trend of paying attention to the topic of the RPL can be divided into three periods. About 75% of documents were published after the 2010 year. In recent years, the publication has increased exponentially. From an overall perspective, the research found that the RPL field has experienced spectacular growth recently.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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