

The Top 100 Most Cited Articles on Intrauterine Adhesion: A Bibliometric Analysis

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Research

Keywords: Intrauterine adhesion, hysteroscopy, hysteroscopic adhesiolysis, bibliometric analysis

Posted Date: April 6th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-345211/v1>

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Version of Record: A version of this preprint was published at Reproductive Sciences on November 15th, 2021. See the published version at <https://doi.org/10.1007/s43032-021-00794-x>.

Abstract

Background: Bibliometric analysis is a statistical method which attempts to assess articles by their citations, analyzing their frequency and pattern of citing phenomenon. Through the analysis, some guidance can be extracted for future research directions. Over the past few years, there have been articles published in mounting numbers focused on intrauterine adhesions. Nevertheless, little is known about the properties and qualities of these researches. No existed analysis commits to reflecting the progress of researches in intrauterine adhesion.

Methods: Web of Science Core Collection, BIOSIS Citation Index and MEDLINE were searched for the identifying articles released from 1950 to October 2020. Articles concerning about Intrauterine adhesion were determined. Subsequently, the 100 most cited articles were chosen for analysis of citation count, citation density (citations/article age), authorship, theme, geographic distribution, time-related flux, level of evidence, and network analysis.

Results: An overwhelming majority of the certain 100 articles were put out in the 2010s (35%). Citations per article ranged from 30 to 253. China possesses the most papers among the top 100 papers, followed by the USA, France, Israel and Italy. The study theme that most highlighted were operative hysteroscopy and adjunctive treatments for improving reproductive outcome. Level II is the most common level of evidence, and there is no statistical difference in the number of citations between the levels. The network analysis connoted that hysteroscopy, hysteroscopic adhesiolysis, infertility, and reproductive outcome had a great degree of centrality in the 2000s and 2010s, while placental implantation had a great degree of centrality in the 2000s and stem cell and fibrosis had a great degree of centrality in the 2010s.

Conclusions: We conducted a bibliometric analysis of the top 100 most cited articles in the literature on intrauterine adhesions. It is worth noting that hysteroscopy and hysteroscopic adhesiolysis were long-term concern in the field of intrauterine adhesion researches. As the elapse of time, postoperative adjuvant treatment has gradually become the hot spot of researches. However, there are only 9 experimental articles among these 100 articles, showing the lack of breakthrough progress in the field of intrauterine adhesions at the mechanism level.

Background

Intrauterine adhesion (IUA) was first defined and reported by Asheman Joseph G in 1950 (1, 2). IUA is caused by mechanical injury or infection hurt to the basal layer of the endometrium, resulting in the formation of fibromuscular or severe connective tissue adhesion of the uterine cavity or cervical canal (3, 4). Hypomenorrhea/ amenorrhea (5), infertility(6), recurrent pregnancy loss (7) and obstetric complications (8) are common complication of IUA. IUA may also lead to low birth weight (9). At present, IUA have become one of the stubborn diseases that seriously affect the reproductive prognosis and quality of lives of women in childbearing age (6, 10).

Surgical treatment is the first choice for IUA. Hysteroscopic adhesiolysis, the standard treatment for IUA, hold the limited therapeutic effect though (11). The conception rate is 25% after hysteroscopic adhesiolysis, and the rate of reformation of adhesions is 20%-63% (12–15). In order to reduce the recurrence rate of IUA and improve reproductive prognosis, it is often recommended to assist other prevention and treatment measures for comprehensive management of adhesions after the surgery (16–18). These measures mainly include devices to keep opposing endometrial surfaces separated, such as intrauterine device (IUD) (19), Foley catheter balloon (20), auto-crosslinked hyaluronic acid (ACP) gel (21–24), and interventions to promote endometrial regeneration, such as estrogen (25, 26), stem cell (27–29), stem cell exosome (30), amniotic epithelial cells (31), granulocyte colony stimulating factor (32), platelet rich plasma (33), aspirin (34), etc. However, current effectiveness is still not ideally. The reformation rate is still as high as 48% (35), the conception rate is about 44.3%, and the live birth rate is 37.8% (36). Therefore, when it comes to IUA, how to reduce the reformation rate of IUA and increase the postoperative conception rate and live birth rate is still the main focus of research.

The aim of this research is to figure out and analyze the 100 most cited essays in the field of IUA, emphasize the research trends and hotspots in this area, and evaluate the research quality and properties of the most cited original papers in the past 70 years. This analysis are supposed to provide some guidance for subsequent research directions.

Methods

Search strategy

All articles were selected by searching the Web of Science Core Collection, BIOSIS Citation Index and MEDLINE to retrieve all articles which have relation to IUA. Searching process was done by two individuals at the same time to upgrade the search sensitivity. The terms used for searching were as follows: “Intrauterine adhesion” OR “Asherman Syndrome”.

The exploring was conducted in October 2020 and yielded a total of 1,999 results. Subsequently, search results were filtered. Only original articles were included. Hence, articles in types of review articles, systematic reviews, meta-analyses, and guidelines were all excluded. In order to the number of screening articles, those articles which were cited less than 10 times were excluded. As a result, 418 articles were included for analysis. Two independent individuals reviewed the title and the abstract of all included articles. Articles that met the following criteria were included: (1) basic study, animal study, and clinical trials related to any aspect of IUA; (2) the clinical therapeutic, prognostic, diagnostic, epidemiological studies of IUA; (3) the case report data of IUA. Disagreement between the two reviewers was discussed to reach an agreement. After the title and abstract review, there were 241 articles remaining. These articles were ranked in descending order of citations and the first 100 most cited articles were included in this analysis (Fig. 1).

Data extraction

All articles were reviewed by two independent well-trained individuals. The following information was listed for all articles: the journal name, publication date, first author, year of publication, geographic origin, total number of citations of the article, overall citation rate (total citations/article age), research theme, and level of evidence (methodology has been described elsewhere(37)).

Statistical analysis

The Shapiro-Wilk test was used to test the distribution of individual variables for normality. Normally distributed data are presented as mean \pm standard deviation. Comparison between means was performed using one way analysis of variance (ANOVA), and post-hoc testing was undertaken when necessary. Time-dependent trends were tested using the Mann-Kendall trend test. Correlation between variables was performed using the Spearman rank or Pearson tests. A $P < 0.05$ was considered to be statistically significant. Analysis was performed using IBM SPSS Statistics, Version 20.0. The Ucinet for windows, version 6.212 was used to perform the degree of centrality analysis(38).

Results

We extracted 100 articles which is cited most in the field of IUA which is listed in Table 1. Citations ranges from 30 to 253 in number, with a majority of them published in the 2010s (35%) and 2000s (29%). The overall trend was increasing year by year (Fig. 2). In 2008, the number of journals reached highest ($n=7$). The number of citations was 6462 generally, 47 (0.7%) in the 1960s, 356 (5.5%) in the 1970s, 721 (11.2%) in the 1980s, 1190 (18.4%) in the 1990s, 2097 (32.5%) in the 2000s, and 2051 (31.7%) in the 2010s. The Mann-Kendall trend test showed no time-dependent trend in the publication time of articles ($P=0.4654$) but an increasing trend between the citation density and the time ($P=2.2E-16$) (Fig. 3). The Spearman rank revealed a positive correlation between time and citation density ($r=0.836$, $P < 2.2E-16$). The Shapiro-Wilk test and the Kolmogorov-Smirnov test both indicated an abnormal distribution of the citation data. The Shapiro-Wilk test indicated significant departures from normality ($p < 0.05$) for all distributions tested.

Tab. 1

List of the 100 top-cited articles in intrauterine adhesion research

Rank	Publication year	Total citation	Title	PMCID
1	1996	253	Frequency of factors associated with habitual abortion in 197 couples	8752606
2	2000	236	Diagnostic accuracy at sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases	10685551
3	1988	204	Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome	3381869
4	2004	137	Effectiveness of auto-crosslinked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic surgery: a prospective, randomized, controlled study	15105384
5	1978	133	Hysteroscopic management of intrauterine adhesions	637078
6	2003	129	Effectiveness of auto-cross-linked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic adhesiolysis: a prospective, randomized, controlled study	12923149
7	2016	119	Autologous cell therapy with CD133+bone marrow-derived stem cells for refractory Asherman's syndrome and endometrial atrophy: a pilot cohort study	27005892
8	2011	117	Endometrial regeneration using autologous adult stem cells followed by conception by in vitro fertilization in a patient of severe Asherman's syndrome	21772740
9	2003	114	A comparison of two adjunctive treatments for intrauterine adhesions following lysis	12834941
10	2014	114	Bone Marrow-Derived Stem Cell (BMDSC) Transplantation Improves Fertility in a Murine Model of Asherman's Syndrome	24819371
11	2008	108	Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome	17681324
12	1999	102	Hysteroscopic treatment of severe Asherman's syndrome and subsequent fertility	10325268
13	2004	99	1000 office-based hysteroscopies prior to in vitro fertilization: feasibility and findings	15119651
14	2010	97	Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome	19455349
15	1998	94	Prevalence of Asherman's syndrome after secondary removal of placental remnants or a repeat curettage for incomplete abortion	9886512

16	2012	93	Comprehensive management of severe Asherman syndrome and amenorrhea	22100167
17	1978	91	Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions	677196
18	1993	90	Incidence of post-abortion intra-uterine adhesions evaluated by hysteroscopy—a prospective study	8473464
19	1997	89	Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility	9418714
20	2008	87	Postoperative adhesiolysis therapy for intrauterine adhesions (Asherman's syndrome)	18571166
21	2010	84	Prevalence of unsuspected uterine cavity abnormalities diagnosed by office hysteroscopy prior to in vitro fertilization	20570971
22	1980	82	Hysteroscopy in the evaluation of female infertility	7386525
23	2006	82	Amnion graft following hysteroscopic lysis of intrauterine adhesions	17100817
24	2006	78	Fertility after treatment of Asherman's syndrome stage 3 and 4	16962521
25	2013	77	A comparison of intrauterine balloon, intrauterine contraceptive device and hyaluronic acid gel in the prevention of adhesion reformation following hysteroscopic surgery for Asherman syndrome: a cohort study	23932377
26	2010	75	Human Amnion as a Temporary Biologic Barrier after Hysteroscopic Lysis of Severe Intrauterine Adhesions: Pilot Study	20576472
27	1995	73	Reproductive outcome following hysteroscopic management of intrauterine septum and adhesions	8567788
28	2004	72	Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or the Versapoint system	15169591
29	2011	72	Hysteroscopic Management of Residual Trophoblastic Tissue Is Superior to Ultrasound-Guided Curettage	22024264
30	2000	71	Predictive value of transvaginal sonography performed before routine diagnostic hysteroscopy for evaluation of infertility	10685552
31	2006	69	Reduction of postoperative adhesions with an auto-crosslinked hyaluronan gel in gynaecological laparoscopic surgery: a blinded, controlled, randomized, multicentre study	16439505

32	1986	68	Severe obstetric complications after aggressive treatment of Asherman syndrome	3703411
33	2013	68	Optimal waiting period for subsequent fertility treatment after various hysteroscopic surgeries	23433831
34	2014	66	Etiology, treatment, and reproductive prognosis of women with moderate-to-severe intrauterine adhesions	24598346
35	2015	66	Human CD133(+) bone marrow-derived stem cells promote endometrial proliferation in a murine model of Asherman syndrome	26384164
36	2009	65	Uterine synechiae after bipolar hysteroscopic resection of submucosal myomas in patients with infertility	18937941
37	2008	64	Efficiency and pregnancy outcome of serial intrauterine device-guided hysteroscopic adhesiolysis of intrauterine synechiae	18774563
38	2010	64	Fertility and pregnancy following pelvic arterial embolisation for postpartum haemorrhage	19832826
39	2003	63	A prospective comparative study between hysterosalpingography and hysteroscopy in the detection of intrauterine pathology in patients with infertility	12696625
40	2004	62	Diagnostic value of hysterosalpingography in the detection of intrauterine abnormalities: A comparison with hysteroscopy	15505312
41	2016	60	Autologous menstrual blood-derived stromal cells transplantation for severe Asherman's syndrome	27664218
42	1981	58	Gestational outcome following hysteroscopic lysis of adhesions	6269905
43	1988	58	Endometrial abnormalities: evaluation with transvaginal sonography	3275446
44	2008	58	Office hysteroscopic early lysis of intrauterine adhesion after transcervical resection of multiple apposing submucous myomas	17686478
45	2013	57	Role of angiogenesis in endometrial repair of patients with severe intrauterine adhesion	23826415
46	2014	57	Effect of stem cell application on Asherman syndrome, an experimental rat model	24974357
47	2007	56	Genital tuberculosis in Indian infertility patients	17362955
48	1984	54	Comparison of diagnostic accuracy of laparoscopy, hysteroscopy, and hysterosalpingography in evaluation of female infertility	6232154

49	1999	54	Transvaginal sonohysterographic evaluation of intrauterine adhesions	10064410
50	2012	52	The effect of collagen-binding vascular endothelial growth factor on the remodeling of scarred rat uterus following full-thickness injury	22136717
51	2007	51	Intrauterine adhesions as a risk factor for failed first-trimester pregnancy termination	17900447
52	2006	50	Successful use of vaginal sildenafil citrate in two infertility patients with Asherman's syndrome	16724891
53	1976	49	Obstetric complications after treatment of intrauterine synechiae (Asherman's syndrome)	934560
54	2011	49	Efficacy of a Polyethylene Oxide-Sodium Carboxymethylcellulose Gel in Prevention of Intrauterine Adhesions After Hysteroscopic Surgery	21777835
55	1979	48	Hysteroscopy in 100 patients	437163
56	2015	48	Randomized, controlled trial comparing the efficacy of intrauterine balloon and intrauterine contraceptive device in the prevention of adhesion reformation after hysteroscopic adhesiolysis	25936237
57	1966	47	The pathology of postcurettage intrauterine adhesions	5928449
58	1998	47	Myometrial scoring: a new technique for the management of severe Asherman's syndrome	9591493
59	2004	47	Hysteroscopy in the evaluation of patients with recurrent pregnancy loss - A cohort study in a primary care population	15809790
60	2016	47	MicroRNA-29b Inhibits Endometrial Fibrosis by Regulating the Sp1-TGF-beta 1/Smad-CTGF Axis in a Rat Model	26392347
61	1981	45	Significance of intrauterine adhesions detected hysteroscopically in eumenorrheic infertile women and role of antecedent curettage in their formation	7468688
62	1985	45	Etiology of cervical pregnancy. Association with abortion, pelvic pathology, IUDs and Asherman's syndrome	4038744
63	2008	44	Placenta Accreta An Association With Fibroids and Asherman Syndrome	18946102
64	2014	44	Does cold loop hysteroscopic myomectomy reduce intrauterine adhesions? A retrospective study	24182410
65	2011	43	Outpatient hysteroscopy: a routine investigation before assisted reproductive techniques?	20638055
66	2013	43	Creation of a female rabbit model for intrauterine	23199550

			adhesions using mechanical and infectious injury	
67	2012	42	Changes in endometrial receptivity in women with Asherman's syndrome undergoing hysteroscopic adhesiolysis	22535194
68	1994	41	Post-abortion-hysteroscopy--a method for early diagnosis of congenital and acquired intrauterine causes of abortions	7713291
69	2015	41	Results of centralized Asherman surgery, 2003-2013	26428306
70	1992	40	Hysteroscopic findings after missed abortion	1521644
71	1993	40	Induced regeneration of endometrium following curettage for abortion: a comparative study	8408501
72	2007	40	Fluoroscopically guided synechiolysis for patients with Asherman's syndrome: menstrual and fertility outcomes	17109860
73	1997	39	Successful treatment of severe uterine synechiae with transcervical resectoscopy combined with laminaria tent	9194644
74	2005	39	Pathologic findings in hysteroscopy before in vitro fertilization-embryo transfer (IVF-ET)	16316847
75	2014	39	Diagnostic accuracy of three-dimensional sonohysterography compared with office hysteroscopy and its interrater/intrarater agreement in uterine cavity assessment after hysteroscopic metroplasty	24581576
76	1989	38	Value of intrauterine device insertion and estrogen administration after hysteroscopic metroplasty	2549238
77	2008	38	Thin unresponsive endometrium-a possible complication of surgical curettage compromising ART outcome	18797990
78	1983	37	Diagnosis and treatment of intrauterine adhesions by microhysteroscopy	6825866
79	2017	37	Prevalence of intrauterine adhesions after the application of hyaluronic acid gel after dilatation and curettage in women with at least one previous curettage: short-term outcomes of a multicenter, prospective randomized controlled trial	28390688
80	2018	37	Allogeneic cell therapy using umbilical cord MSCs on collagen scaffolds for patients with recurrent uterine adhesion: a phase I clinical trial	29996892
81	2010	36	Results of 2500 office-based diagnostic hysteroscopies before IVF	20207586
82	2017	36	Reproductive Outcomes in Patients With Intrauterine Adhesions Following Hysteroscopic Adhesiolysis:	27856386

Experience From the Largest Women's Hospital in China

83	2017	36	Effects of Aspirin and Intrauterine Balloon on Endometrial Repair and Reproductive Prognosis in Patients with Severe Intrauterine Adhesion: A Prospective Cohort Study	28251159
84	1976	35	Intrauterine adhesions secondary to elective abortion. Hysteroscopic diagnosis and management	
85	1992	35	Diagnostic hysteroscopy: its value in an in-vitro fertilization/embryo transfer unit	1291572
86	1996	35	Hysteroscopic management of uterine synechiae: a series of 102 observations	8730623
87	1999	35	Fluoroscopically guided hysteroscopic division of adhesions in severe Asherman syndrome	10362178
88	2000	35	Operative hysteroscopy for infertility using normal saline solution and a coaxial bipolar electrode: a pilot study	10920101
89	2007	35	Prevalence of uterine synechia after abortion evacuation curettage	18094891
90	2008	35	Genital tuberculosis: an important cause of Asherman's syndrome in India	17653564
91	2016	35	Endometrial stem cells repair injured endometrium and induce angiogenesis via AKT and ERK pathways	27486270
92	2015	34	Preventive effect of oral mucosal epithelial cell sheets on intrauterine adhesions	25475585
93	2007	33	Hysteroscopy after uterine fibroid embolization in women of fertile age	17578361
94	2016	33	The influence of the location and extent of intrauterine adhesions on recurrence after hysteroscopic adhesiolysis	25753391
95	2017	33	Human amniotic mesenchymal stromal cell transplantation improves endometrial regeneration in rodent models of intrauterine adhesions	28285950
96	1982	32	Asherman's syndrome. A comparison of therapeutic methods	7120210
97	1995	31	Preoperative sonographic measurement of endometrial pattern predicts outcome of surgical repair in patients with severe Asherman's syndrome	7843453
98	1996	31	Intrauterine adhesions: detection with transvaginal US	8638001
99	1999	31	Total corporal synechiae due to tuberculosis carry a very poor prognosis following hysteroscopic	10438408

synechialysis				
100	1997	30	Simplified therapy for Asherman's syndrome	9418695

These articles were distributed in 22 countries (Fig. 4), led by China (n=19) followed by the USA (n=18), France (n=8), Israel (n=8), and Italy (n=8). The allocation is presented on the world map (Fig. 5). In terms of regional distribution, most of the articles published from two countries: America and Asia. The rest were scattered in Europe, Africa and Oceania. Developed countries accounted for 67% of all countries mentioned above. Articles were all published in 33 journals, among which 27 articles were published in "Fertility and sterility", followed by "Human Reproduction" (n=16), American journal of obstetrics and gynecology" (n=6), "Journal of Minimally Invasive Gynecology" (n=5). (Table 2).

Tab. 2

Journals of the 100 top-cited studies published.

Publication	Number account	Total citation	Average citation	IF (2020)
Fertility and sterility	27	1895	70	6.3
Human Reproduction	16	1171	73	5.7
American journal of obstetrics and gynecology	6	602	100	6.5
Journal of Minimally Invasive Gynecology	5	310	62	3.1
Obstetrics and Gynecology	4	187	47	5.5
Archives of Gynecology and Obstetrics	3	174	58	2.3
European journal of obstetrics, gynecology, and reproductive biology	3	153	51	1.9
International Journal of Gynecology & Obstetrics	3	236	79	2.2
Journal of Obstetrics and Gynaecology Research	3	178	59	1.4
The Journal of reproductive medicine	3	115	38	0.2
Bjog-an International Journal of Obstetrics and Gynaecology	2	97	49	4.7
Journal of Assisted Reproduction and Genetics	2	95	48	2.8
Reproductive Biomedicine Online	2	108	54	3.2
AJR. American journal of roentgenology	1	58	58	3.0
American Journal of Roentgenology	1	62	62	3.0
Biomaterials	1	52	52	10.3
Biomed Research International	1	36	36	2.3
Contraception	1	51	51	2.8
Cytotherapy	1	33	33	4.2
Gynecological Endocrinology	1	39	39	1.6
International Journal of Clinical and Experimental Pathology	1	57	57	0.3
Journal of human reproductive sciences	1	54	54	0.8
Journal of Clinical Ultrasound	1	117	117	1.0
Journal of Surgical Research	1	43	43	1.8
Journal of Ultrasound in Medicine	1	44	44	1.8
Journal of Womens Health	1	50	50	1.9

JSLs: Journal of the Society of Laparoendoscopic Surgeons	1	99	99	1.5
Plos One	1	114	114	2.7
Radiology	1	31	31	7.9
Reproduction	1	35	35	3.2
Reproductive Sciences	1	47	47	2.6
Sao Paulo Medical Journal	1	35	35	1.0
Stem Cell Research & Therapy	1	37	37	5.1
Surgical Endoscopy and Other Interventional Techniques	1	47	47	3.1

Among the 100 highly cited articles, 10 researchers have more than two articles which is listed in Table 3. These authors' articles are all clinical studies related to IUA. Among them, CM March and Jehn-Hsiahn Yang had 3 first authorships mainly in the field of IUA. CM March's focus was on hysteroscopic adhesiolysis, and Jehn-Hsiahn Yang's research direction was endometrium regeneration. Although R F Valle from the United States had only two articles, the number of citations is relatively high, with an overall number of citations of 286. Auxiliary diagnosis of IUA is his main focus.

Tab. 3

List of first authors with frequent articles within the top-cited list.

First Author	Number of Study	Citations Account	Author's Affiliation
C M March	3	226	Department of Obstetrics and Gynecology, University of Southern California School of Medicine Los Angeles, California, USA.
Jehn-Hsiahn Yang	3	159	Department of Obstetrics and Gynecology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan.
R F Valle	2	286	Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago, Illinois, USA
Mohamed I Amer	2	157	Department of Obstetrics and Gynecology, Ain Shams University, Cairo, Egypt.
Recai Pabuccu	2	153	Department of Obstetrics and Gynecology, Gülhane School of Medicine, Ankara, Turkey.
Xiaona Lin	2	125	Center of Reproductive Medicine, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, PR China.
H Fernandez	2	113	Department of Obstetrics and Gynaecology, Antoine Bécclère Hospital, Clamart Cedex, France.
Yuqing Chen	2	93	Department of Obstetrics and Gynecology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.
P J Taylor	2	93	Department of Obstetrics and Gynecology, University of Calgary and Foothills Hospital, Calgary, Alberta, Canada
A Golan	2	75	Department of Obstetrics and Gynecology, Assaf Harofeh Medical Center, Zerifin, Israel.

The 100 most cited articles mainly focus on the following themes: auxiliary treatment of IUA (n = 28), prognosis of IUA (n=19), incentive factors of IUA (n=16), hysteroscopic adhesiolysis (n=14), evaluation methods for IUA (n=12), complications of IUA (n = 6), relevant mechanism of IUA (n = 4), new devices for IUA (n=1). The most mentioned theme was the adjuvant treatment of IUA, followed by the reproductive prognosis of patients after hysteroscopic adhesiolysis (Fig. 6). One-way ANOVA revealed no significant difference in citations per article among the various themes (Fig. 7). Nevertheless, the impact factor of article from different themes was statistically different (P=0.012) (Fig. 8).

In terms of the level of article evidence, the level II (n=39) category has a mean number of 69 ± 48 citations per article, making up the largest number. The level I (n=23) category has a mean number of 63 ± 30 citations per article, the level IV (n=14) with 48 ± 22 citations. Difference in citations per article between different levels of evidence is not significant analyzed by one-way ANOVA (Fig. 9).

Network analysis of the key words or subject terms has been done in two periods of article published time: in the 2000s (34 articles) and in the 2010s (30 articles). The result indicated that "hysteroscopy", "hysteroscopic adhesiolysis", "infertility", and "reproductive outcome" possessed a high degree of centrality in the 2000s and 2010s, while "placenta accrete" were greatly centralized in the 2000s and "stem cell" and "fibrosis" was highly concentrated in the 2010s (Fig. 10-11).

Discussion

This is the first bibliometric analysis of papers in the field of IUA. Mass of interesting findings can be drawn from this analysis of the top 100 most cited papers published on IUA in the past 70 years. Not only the papers which had made important contributions to the progress in this field were reflected, but also current development trend was revealed. Generally speaking, with the time goes by, the number of citations of papers would be piled up. However, it is contrary to expectation that the number of articles was gradually increasing as time progresses when we assessed the certain 100 most cited articles according to the division of each decade. Articles in 2010s possessed the highest proportion, reaching 35%. As time increases, not only the proportion of articles presented an growing trend, but also the citation density, that is, the number of citations divided by the number of years of publication, figured an increasing trend. On the one hand, this reflects the "obliteration by incorporation" (39), that is, the citations of the original work decreased with the passage of time for familiarity during the long-term and widespread use, and new findings replaced them. On the other hand, this also presented the phenomenon that the diagnosis, treatment and advanced researches related to IUA have been paid more and more attention by the international community. In addition, 91% of these articles were clinical studies, and only 9% were basic experimental studies. Those basic studies mentioned above were all published in the 2010s. We may say that clinical research has always been the focus of researchers in the field of IUA. However, the disease mechanism is also crucial to the treatment of the disease. Current researches on the mechanism had an increasing trend, and it has the potential to provide clinical directions in the future.

Different from the trend of other bibliometric analysis reports, articles originating from the United States and developed countries did not have an absolute advantage. China and the United States were both important sources of articles, with 19 and 18 articles respectively. 33% of the 100 most cited papers were from developing countries, 67% were from developed countries. There are several reasons for this condition: (1) The clinical manifestations of IUA were first reported in the United States in the 19th century, and later defined and named by American doctors. Therefore, they were able to study it earlier and more systematically (40); The United States and other developed countries had sufficient funds to support scientific research. The sharing of these research results will help the progress of researches on IUA (41, 42); (2) As we all know, the occurrence of IUA is closely related to abortion and curettage. Honestly, abortion is considered illegal in many developing countries due to religious beliefs. In developed countries, the rate of abortion dropped by 19 percentage points from 1990 to 2014, while it only fell by 2 percentage points in developing countries (43). Moreover, least-safe abortions accounted for the largest proportion in developing countries (44); (3) China and other developing countries had great population. Propaganda and popularization of contraceptive measures were inadequate. It was inevitable to choose

surgical abortion after unintended pregnancy. Repeated or informal intrauterine operations may finally lead to irreversible hurt to endometrium (45, 46); (4) After China opened up the two-child policy, more and more IUA were discovered, and recurrent IUA need to be treated (47, 48). IUA is a universal disease, but unfortunately, no multinational cooperation work was found in these 100 most cited papers.

Actually, the impact factors of journals were not high. This was because related papers were rarely published in comprehensive journals, while the impact factors of obstetrics and gynecology professional journals are relatively low. This result highlighted a growing tendency that researchers may prefer to publish articles in influential professional journals. However, there was no denying that the value of IUA researches have not been highly appreciated.

Nearly 50% of the certain 100 papers were issued in two journals, "Fertility and sterility" and "Human Reproduction", followed closely by two heavyweight journals in the field of obstetrics and gynecology, "American journal of obstetrics and gynecology" and "Obstetrics and Gynecology". This demonstrated that IUA were particularly concerned in the field of reproductive medicine. Among the 100 most cited articles, the themes of papers published in recent years appeared to be more diverse, including the Phase I clinical study of autologous stem cell transplantation for the treatment of IUA published in Stem Cell Research & Therapy (49), and collagen scaffold for endometrial regeneration published in Biomaterials (50).

When it comes to the first author of the 100 most cited papers, we found that 2 researchers contributed 3 articles. One of them was Charles M. March from the United States. His articles were all published before 1990, and emphasized that hysteroscopy is the gold standard for diagnosis and classification of IUA, and hysteroscopic adhesiolysis is the first choice for the treatment of IUA (51–53). The other one was Jehn-Hsiahn Yang from Taiwan, China, a younger generation of researchers. The similarity with Charles M. March was that they both focus on hysteroscopy. His three articles have proposed that IUA was common complications after transcervical resection of multiple apposing submucous myomas (54), the formation of new adhesions after hysteroscopic adhesiolysis was the reason that affects endometrial repair (55), the location and area of adhesions were important factors that affect the recurrence of IUA (15).

The level of evidence was between I and V. The overall distribution was average, and level II was relatively high, which is distinct with other bibliometric-related studies. This may attribute to the design of clinical trials. Treatment of IUA was closely related to patients' reproductive prognosis, and for women, age was also a significant factor. Therefore, considering the effect of placebo control on patients, experimental studies are mostly unilateral. In the future, with the increase in the demand for childbirth and the introduction of two or even three-child opening policies in some countries, it is expected that hysteroscopic adhesiolysis, postoperative adjuvant treatment and related research articles will increase more rapidly.

We also studied the theme distribution of articles. The adjuvant treatment of IUA ranked first, followed by the prognosis of reproductive outcome after hysteroscopic adhesiolysis, the incentive factors of IUA, hysteroscopic adhesiolysis and the evaluation method of IUA. Hysteroscopic adhesiolysis is the primary

treatment method. However, how to improve the therapeutic effect through drugs and biological agents after the surgery has been a problem that researchers want to overcome in recent years (56). Network analysis of the author's key words or subject terms has been done in two periods of article published time: in the 2000s (34 articles) and in the 2010s (30 articles). The result indicated that "hysteroscopy, hysteroscopic adhesiolysis, infertility and reproductive outcome" was highly centralized in both 2000s and 2010s and placental implantation was highly concentrated in the 2000s. This was consistent with the research trend in recent years. Researchers have gradually realized that even if patients with IUA succeed in conception, there would be many risks of pregnancy complications. The most cited article in this study was also an article about IUA complications, in which the author proposed that patients with IUA were associated with many risks during pregnancy. An analysis of the citation density of papers published in the 2010s, we found each theme was evenly distributed. In the analysis of the impact factor under each theme, it could be seen that articles related to devices and materials were relatively high, while researches on mechanism were relatively low. Stem cell and fibrosis were highly concentrated in the 2010s. In recent years, researchers have paid more and more attention to the effectiveness of adjuvant therapy after hysteroscopic adhesiolysis in suppressing reformation of adhesion and promoting endometrial regeneration (57). Previous researches focused on placement of uterine stents, foley catheters, hyaluronic acid or hormone replacement therapy (58). Nevertheless, more importance was attached to biotherapy, especially in the field of stem cell therapy. Bone marrow mesenchymal stem cells (BMSC) (59), umbilical cord mesenchymal stem cells (UCMSC) (60), and menstrual blood mesenchymal stem cells (MbMSC) (61, 62) have been used clinically in patients with IUA, resulting in an improvement in reproductive outcome. Researchers reported that the stem cells can promote endometrial cells proliferation, especially inhibit the process of fibrosis (63). In 2020, a review brought together the controversies of different researchers on the treatment of IUA (64). One believed that the adjuvant treatment after the surgery should be paid attention to, and another believed that IUA should be treated with multiple operations. However, it cannot be ignored that, hysteroscopic adhesiolysis has always been the center of research over the years, and the discussion of surgical methods and surgical techniques was still a vacancy (65) It is undeniable that the combined effective adjuvant treatment after surgery is the trend of IUA treatment.

This analysis does generate some valuable information, but it still has some restrictions. First of all, the citation analysis was mainly based on Web of Science. The number of citations may be misleading. Meanwhile, we may miss some important papers that were not included in the SCI database. Secondly, we may overlook the newly published articles that were meaningful in this area but have yet to reach high citation levels owing to the criterion that papers were sorted by the number of citations. All in all, it was by no means exhaustive, but the list of most cited articles still includes many influential papers in the field of IUA.

Conclusion

This article highlights the top 100 most cited articles in the IUA over the last 70 years, including their publication time and regional centers, first author, level of evidence, as well as their research theme. We

revealed the spotlights and properties of studies about IUA since 1950 to 2020. Furthermore, this article sheds light on the notion that postoperative adjuvant therapy played a key role in the field of IUA, and more and more basic and clinical studies are exploring suitable and effective adjuvant treatments for IUA. Meanwhile, the method and techniques of surgical therapy is also controversial. However, the current prognosis of IUA was extremely poor. The tough problem still remains to be solved. Researchers extremely focused on the clinical trial rather than the basic laboratory research. Thus, the foremost difficult is to conquer the situation that little is known about underlying mechanisms of adhesion formation in the uterine and influencing factors.

Abbreviations

IUA: intrauterine adhesion

IUD: intrauterine device

ACP: auto-crosslinked hyaluronic acid

BMSC: bone marrow mesenchymal stem cells

UCMSC: umbilical cord mesenchymal stem cells

MbMSC: menstrual blood mesenchymal stem cells

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by the National Key Research and Development Program of China (grant no. 2018YFC1004800).

Authors' contributions

DX contributed to the design of the study and revise the manuscript. PG and WL contributed to the process of searching, selecting and drafting the manuscript.

Acknowledgements

Not applicable

Footnotes

Not applicable

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Figures

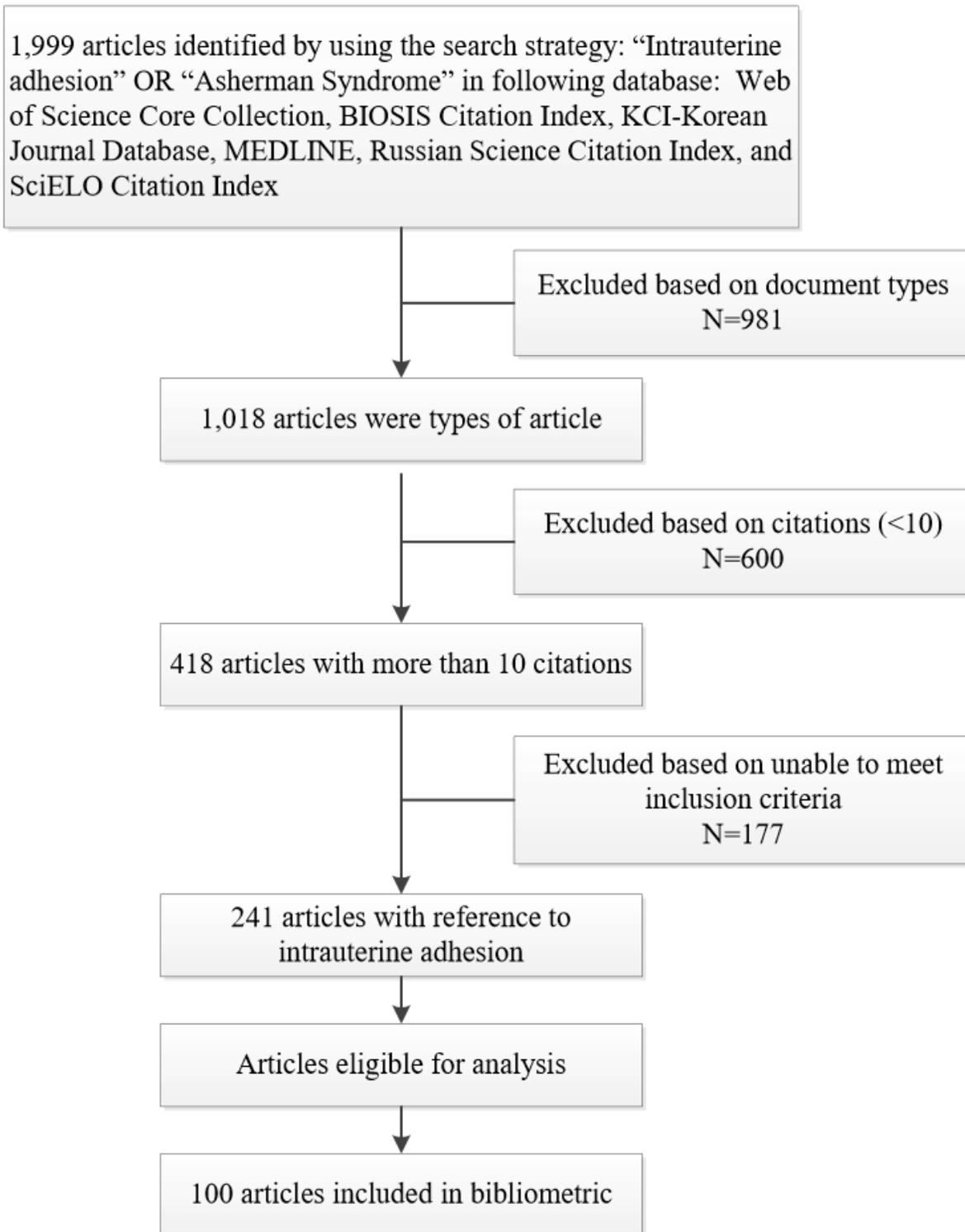


Figure 1

Flowchart illustrating the process of allocation of articles

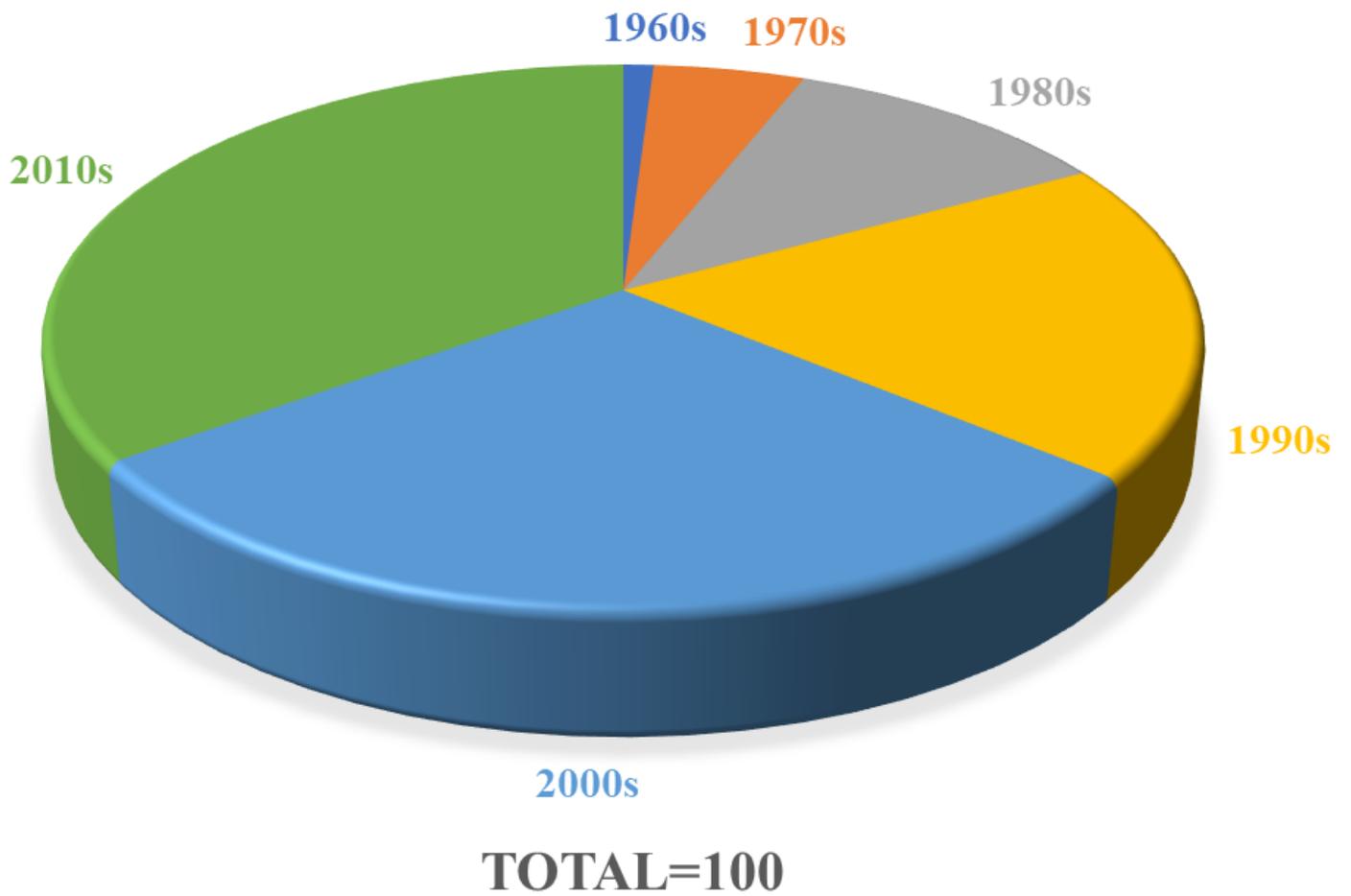


Figure 2

Time distribution of 100 top-cited articles in intrauterine adhesion

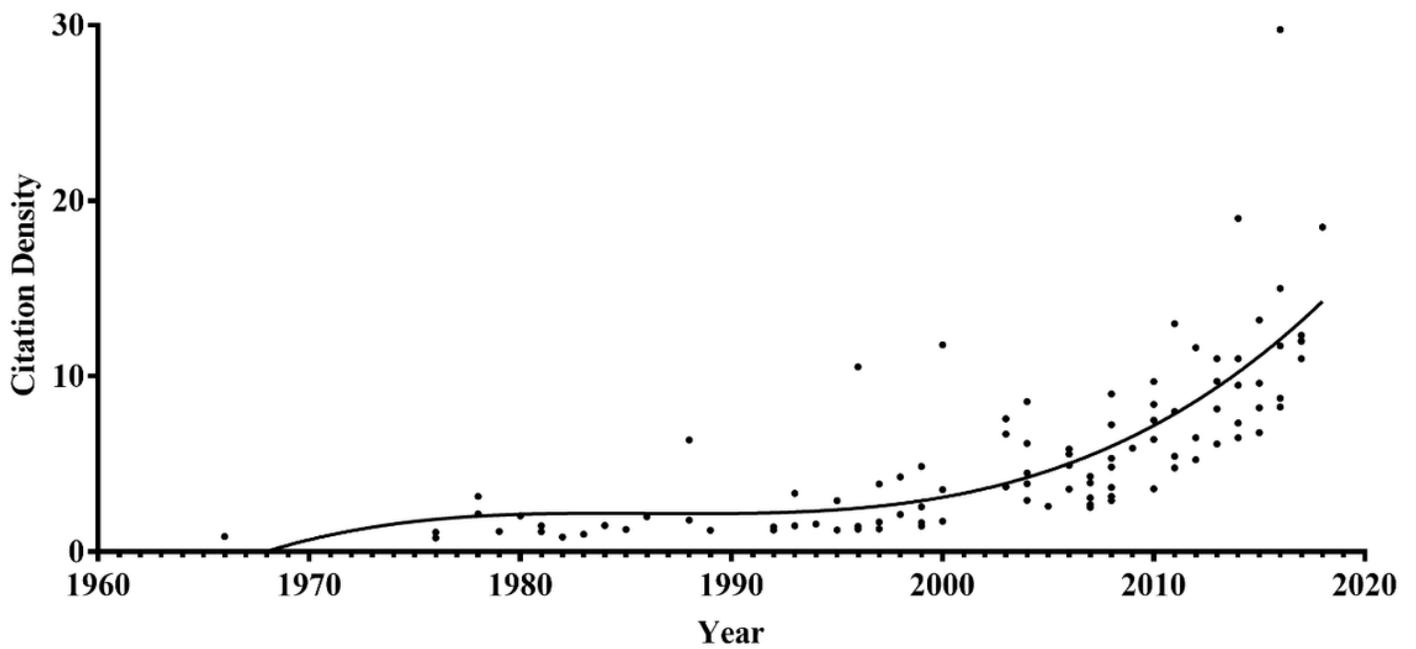


Figure 3

Time-dependent citation density trend of 100 top-cited articles in intrauterine adhesion

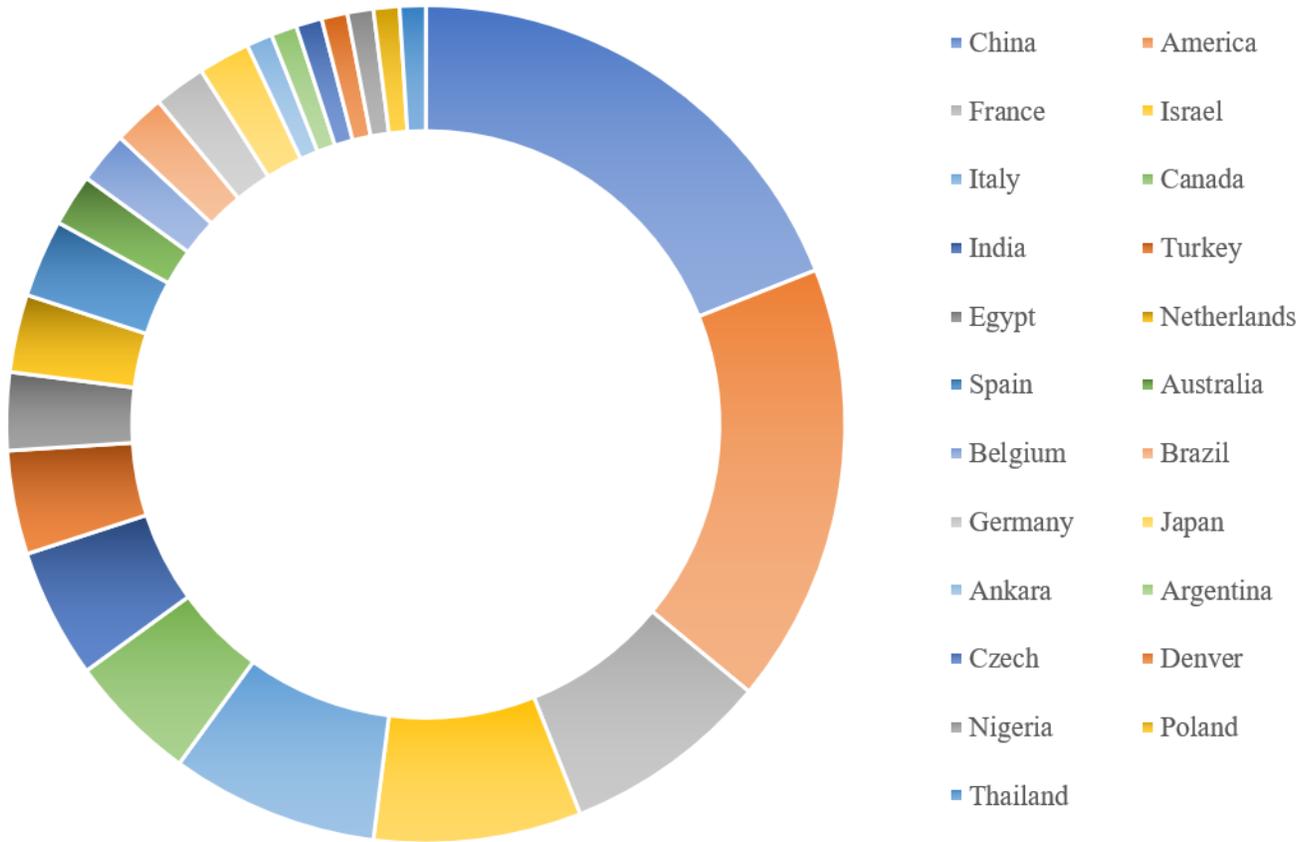


Figure 4

Countries of 100 top-cited articles in intrauterine adhesion

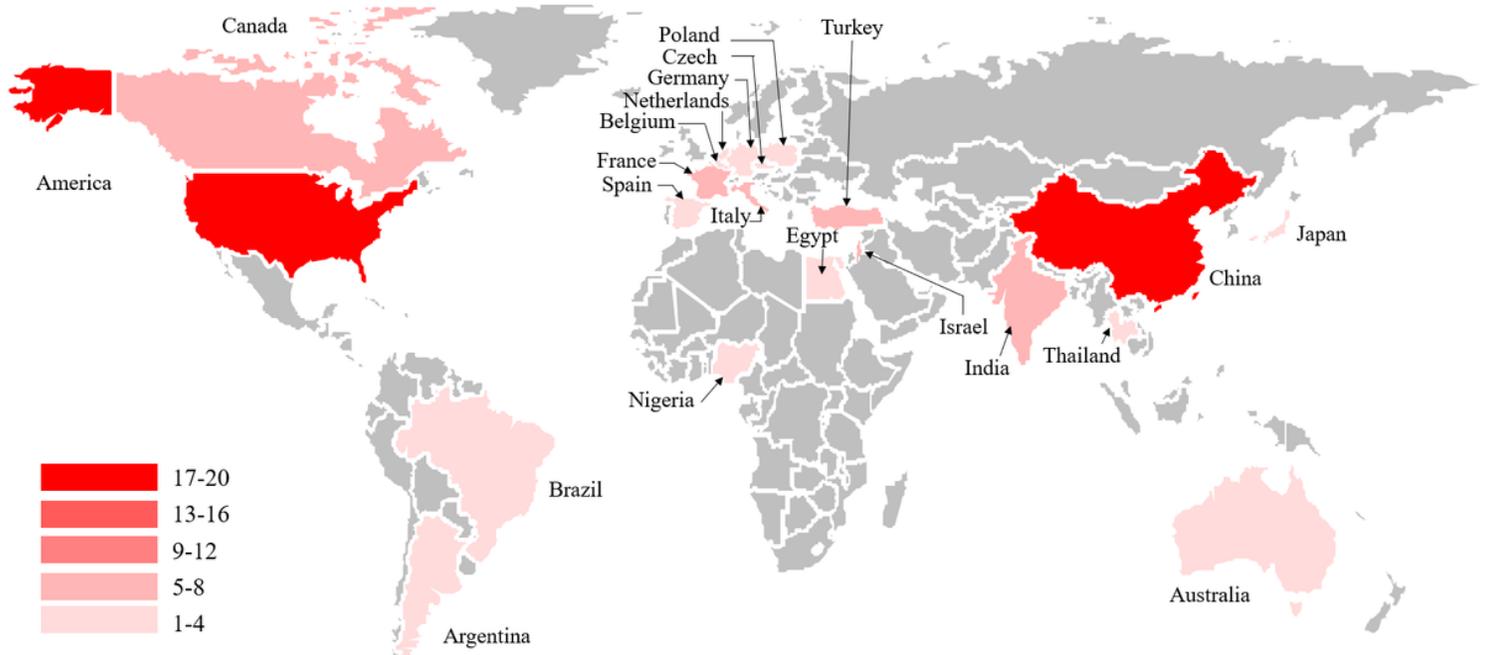


Figure 5

Geographical distribution of 100 top-cited articles in intrauterine adhesion Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

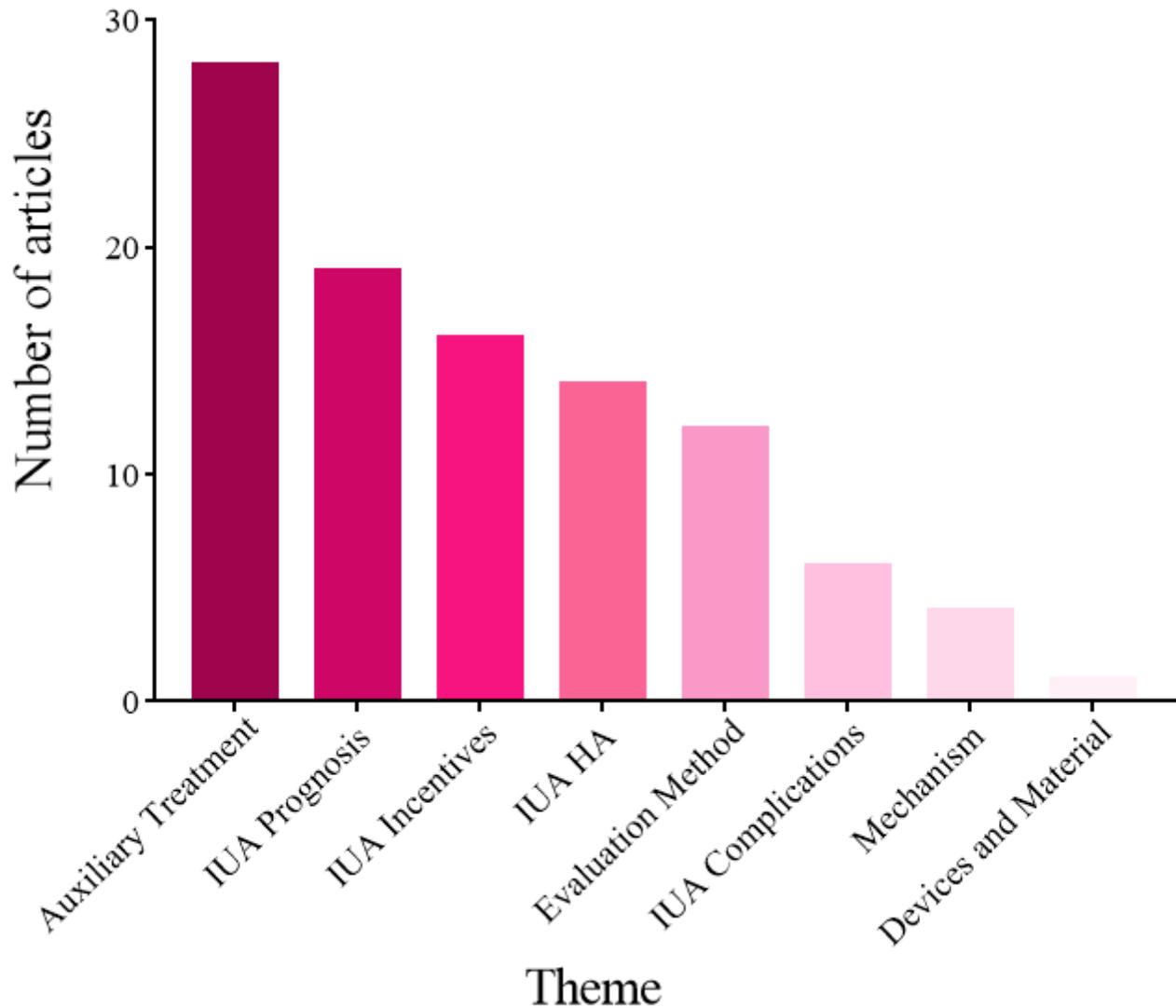


Figure 6

The themes distribution of 100 top-cited articles in intrauterine adhesion

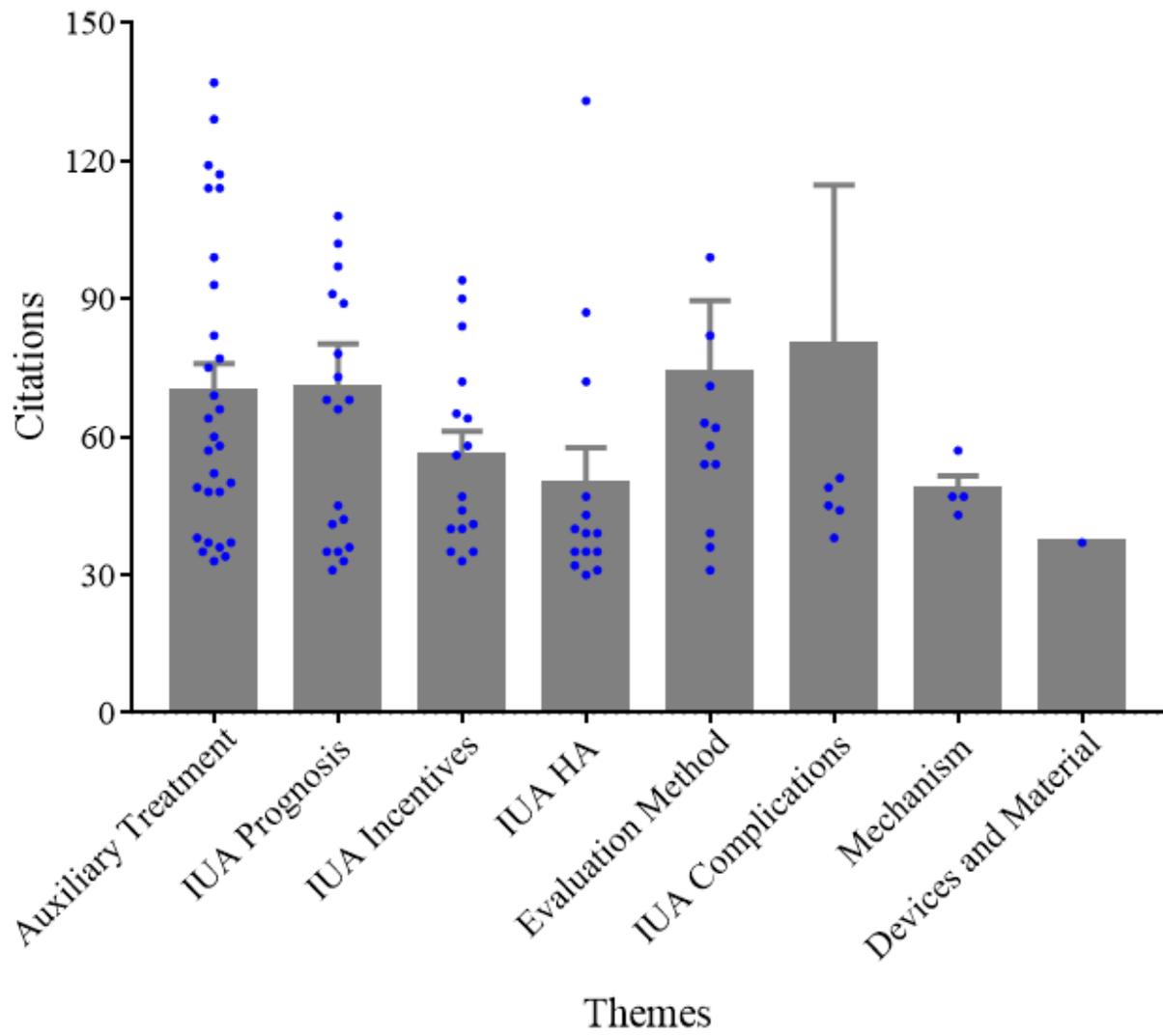


Figure 7

Mean citation per article based on theme

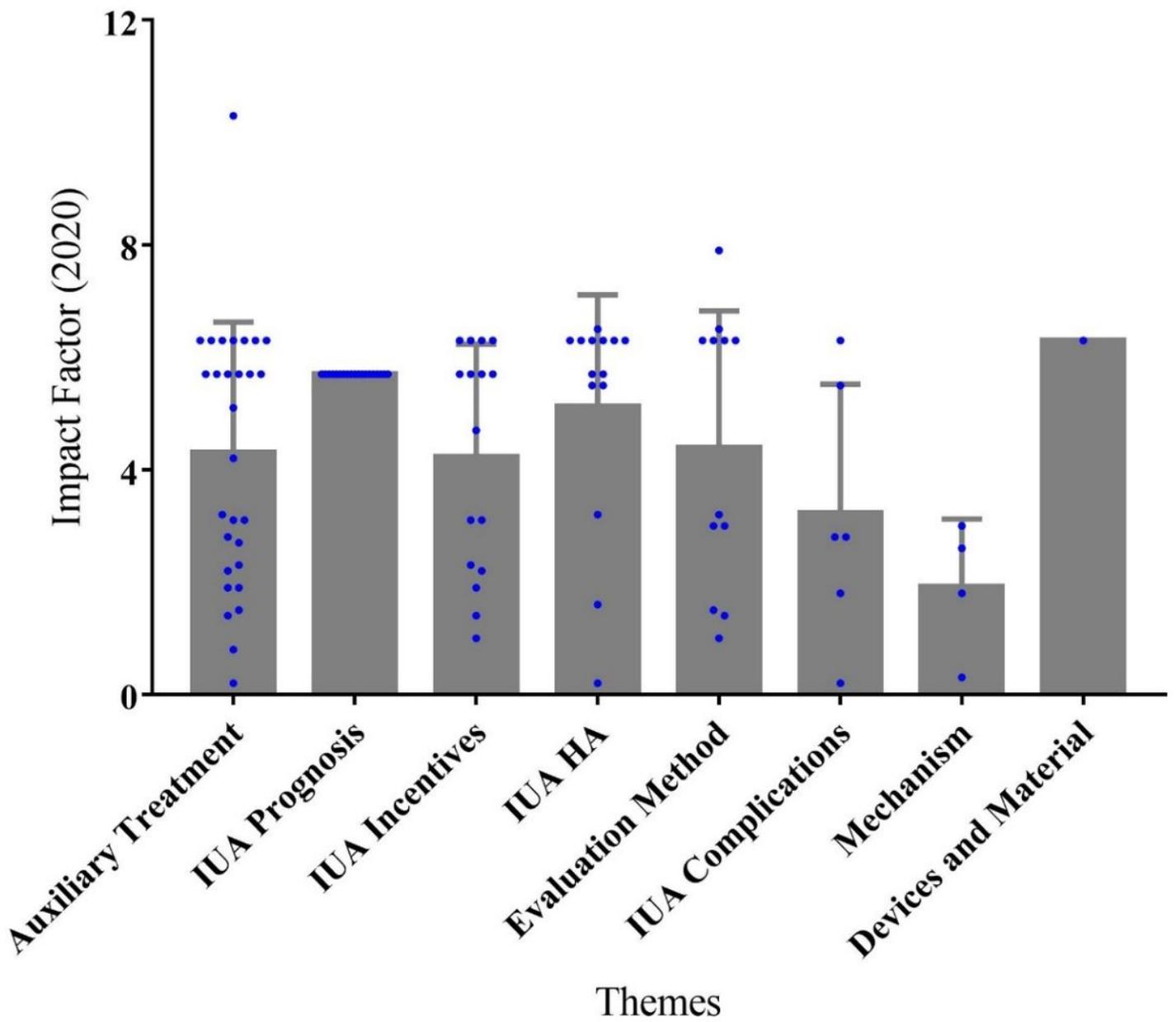


Figure 8

Mean impact factor per article based on theme

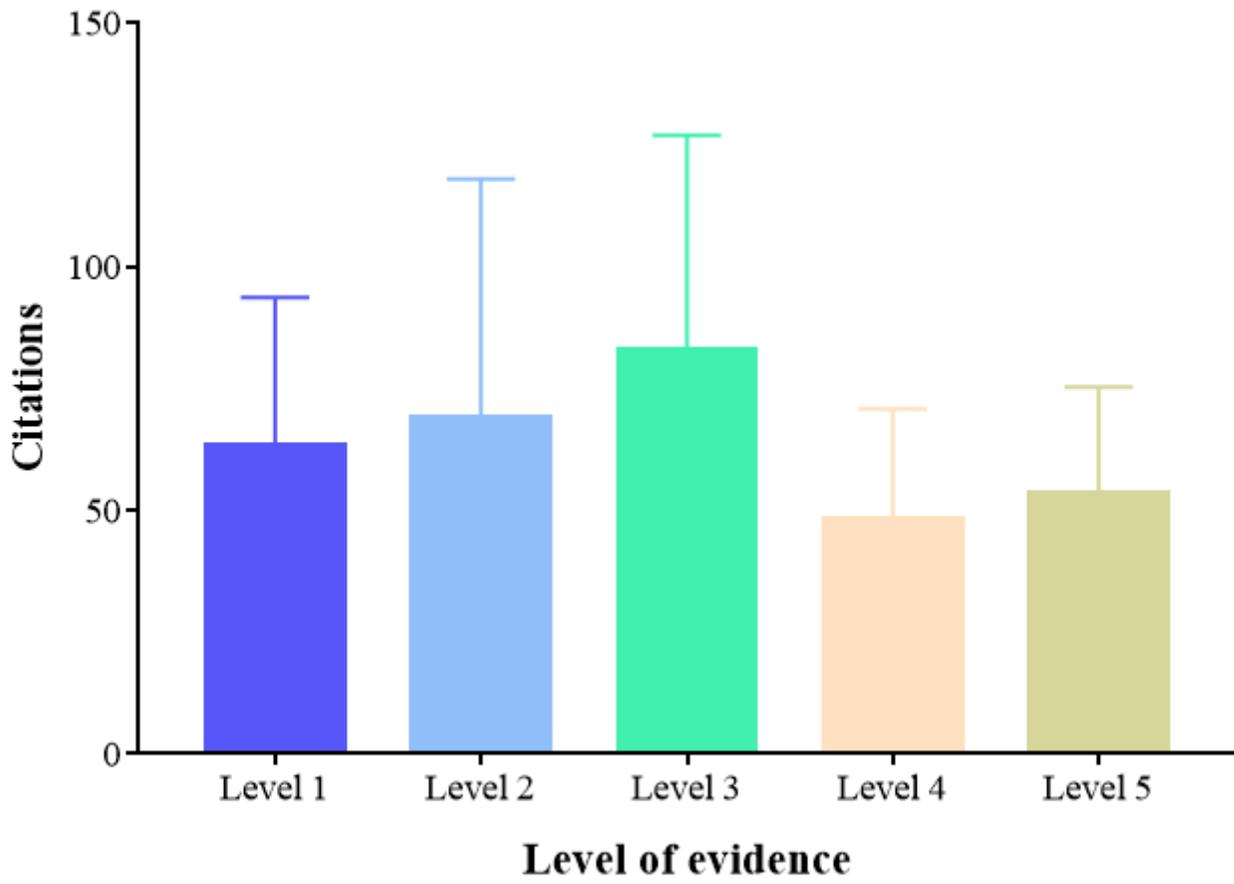


Figure 9

Mean citation per article based on level of evidence

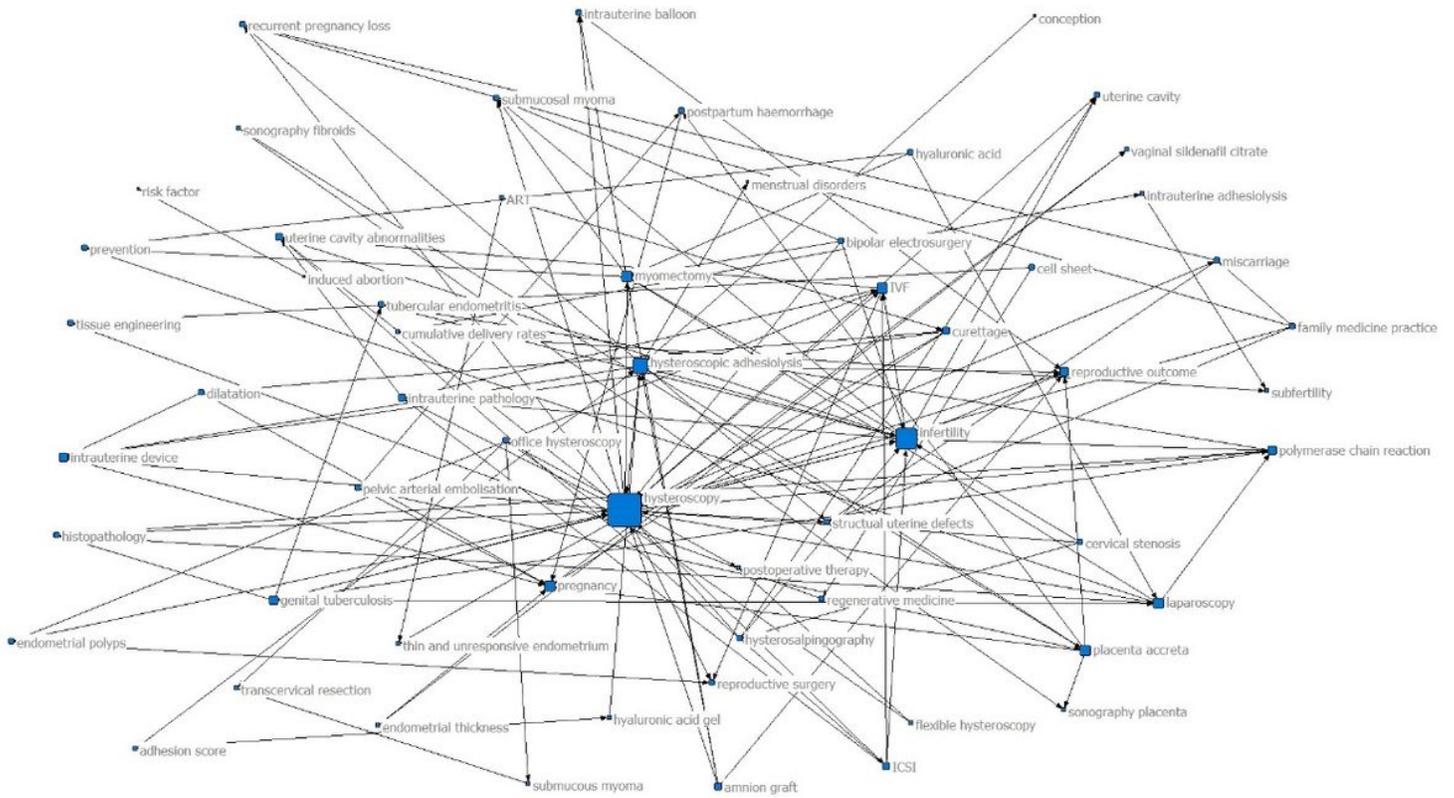


Figure 10

Degree centrality analysis in the 2000s (34 articles)

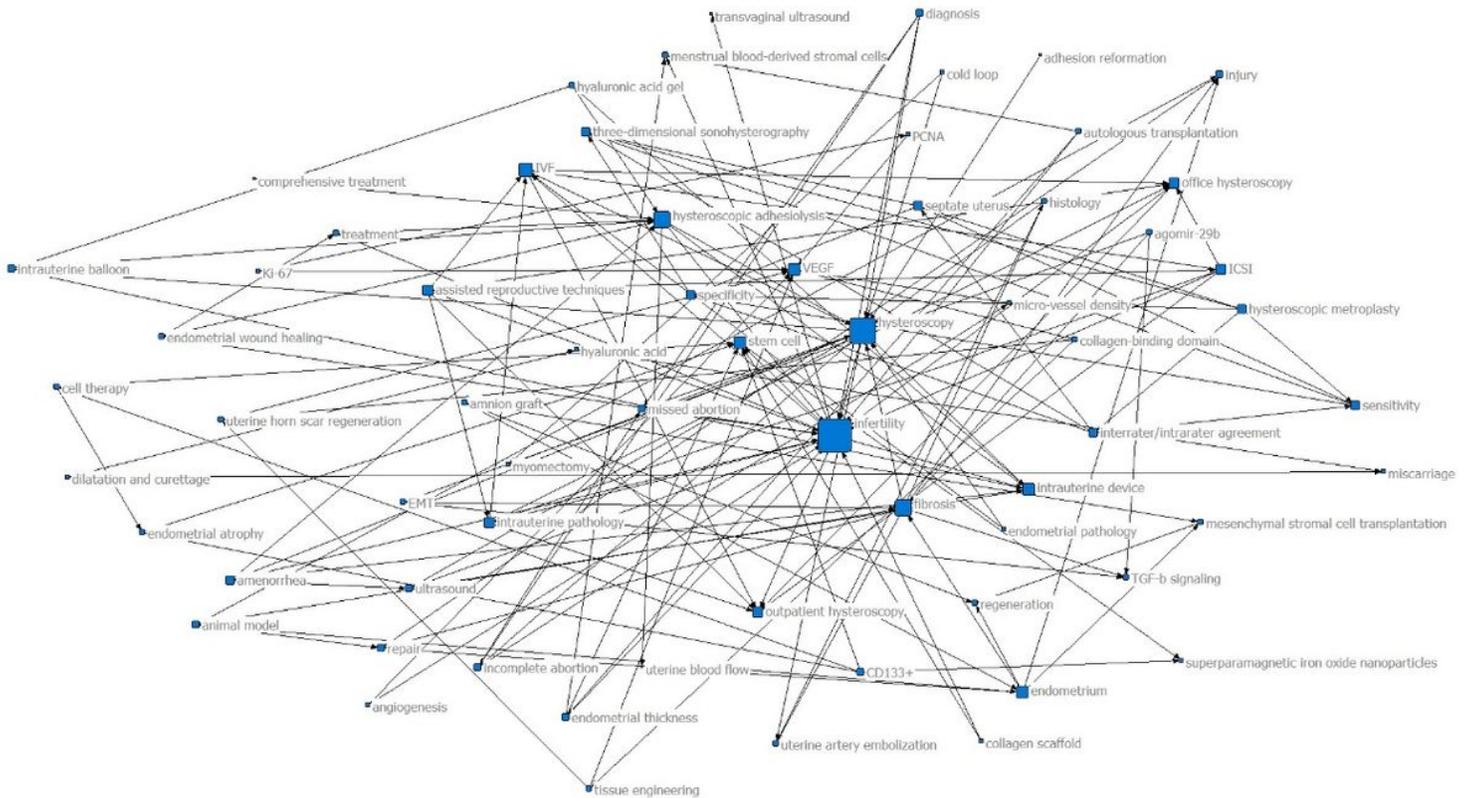


Figure 11

Degree centrality analysis in the 2010s (30 articles)