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A scientometric analysis of research publications on male infertility and assisted reproductive technology

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Abstract

Assisted reproductive technologies (ART) are considered as one of the primary management options to address severe male factor infertility. The purpose of this study was to identify the research trends in the field of male infertility and ART over the past 20 years (2000-2019) by analysing scientometric data (the number of publications per year, authors, author affiliations, journals, countries, type of documents, subject area and number of citations) retrieved using the Scopus database. We used VOS viewer software to generate a network map on international collaborations as well as a heat map of the top scientists in this field. Our results revealed a total of 2,148 publications during this period with Cleveland Clinic Foundation contributing the most (n = 69). The current scientometric analysis showed that the research trend on ART has been stable over the past two decades. Further in-depth analysis revealed that density gradient centrifugation (46%) and intracytoplasmic sperm injection (59.2%) are the most reported techniques for sperm separation and ART, respectively. Additionally, azoospermia was the most studied clinical scenario (60.6%), with majority of articles reporting pregnancy rate (47.25%) as the primary reproductive outcome for ART. This study provides insight into the current focus of research in the area of male infertility and ART as well as the areas that require further research in future.

KEYWORDS

assisted reproductive technique, male infertility, publications, research trend, scientometric analysis

1 | INTRODUCTION

Retrospectively defined as the lack of conception following 1 year of regular unprotected intercourse (World Health Organization, 2010), infertility is reported to affect 10%-15% of couples of reproductive age globally (Agarwal, Mulgund, Hamada, & Chyatte, 2015; Luke, 2017). Although there is a significant variation in the prevalence of male infertility based on geographical and ethnical differences, male partners have been reported to contribute to 20%-70% of couple infertility cases (Agarwal et al., 2015). Reportedly, around 7.5% of men seek advice for infertility concerns, and clinical investigation most commonly reveals abnormal sperm parameters or varicocele (Anderson, Farr, Jamieson, Warner, & Macaluso, 2009). In this context, assisted reproductive technology (ART) has become a popular intervention for male infertility when natural pregnancy can not be achieved (Nayan, Punjani, Grober, Lo, & Jarvi, 2018; Tournaye, 2012). In the United States (USA), the application of ART procedures has increased significantly (198%) from 99,629 in 2000 (Wright, Schieve, Reynolds, & Jeng, 2003) to 197,706 in 2016 (Sunderam et al., 2019), with an estimate of 2.0% of American babies born through ART (https://www.cdc.gov/art/artdata/index.html). It is estimated that almost 0.1% of the current world population was conceived by ART, and this figure is expected to significantly expand to 1.4% of the global population by 2100 (Faddy, Gosden, & Gosden, 2018). Intrauterine insemination (IUI) is considered as the first-line fertility treatment in couples with a motile sperm count of around 5×10^6 spermatozoa and with absence of female reproductive issues. If there is no successful pregnancy following 3-6 IUI cycles, in vitro fertilization (IVF) is then considered (Tournaye, 2006, 2012). Although IUI and IVF have revolutionised the management of infertility, success rate remains poor in cases of abnormal semen quality (Stephens, Arnett, & Meacham, 2013). The advent of intracytoplasmic sperm injection (ICSI) in 1992 (Palermo, Joris, Devroey, & Van Steirteghem, 1992) subsequently allowed for a single sperm injection to be performed. This is particularly recommended when $<0.5 \times 10^6$ spermatozoa are retrieved from the ejaculate or in case of testicular biopsy (Tournaye, 2006, 2012).

Scientometrics is a quantitative analysis of the published literature that aims to shed light on the growth of a specific field of study through the evaluation of bibliometric data (Baskaran et al., 2019; Maula, Fuad, & Utarini, 2018). Previous scientometric studies on male infertility suggested an increase in the research focus on this field (Aleixandre-Benavent, Simon, & Fauser, 2015; Baskaran et al., 2019; Makkizadeh & Bigdeloo, 2019; Zhang et al., 2016). Baskaran et al. (2019) reported an exponential increase in male infertility research over the past 20 years, from 3,311 articles published in 1998 to 8,772 articles published in 2017. Recently, Garcia et al. analysed more than 26,000 articles on ART and couple infertility published between 2005 and 2016, and reported 'male factor' as the second largest macro-category, next to techniques in the field of human ART (Garcia et al., 2019). Furthermore, the impact of sperm DNA fragmentation in ART research is also reportedly receiving increased attention (Baskaran et al., 2019).

Though the application of ART in the clinical management of male infertility has gained importance in recent years, an in-depth analysis of the research trends in this topic is currently lacking. Therefore, this study aims to conduct a detailed analysis of publications based on male infertility and ART, focusing on four major domains related to ART: (a) the procedures carried out for sperm preparation, (b) ART techniques, (c) male infertility-related clinical scenarios, and (d) reproductive outcomes.

2 | MATERIALS AND METHODS

2.1 | Ethical statement

This study was performed on scientometric data retrieved from Scopus and did not involve the participation of any human subjects. It is therefore considered to be excluded from review by the Institutional Review Board.

2.2 | Data source

The current scientometric analysis, as in our previous publications (Agarwal, Baskaran, Panner Selvam, Barbarosie, & Master, 2020; Baskaran et al., 2019), was conducted using Scopus, one of the most inclusive databases of bibliographic data, with over 70 million records, 1.4 billion cited references dating back to 1970 and 16 million authors profiles (https://www.elsevier.com/solutions/scopus/how-scopus-works/content). Scopus metrics (the number of publications per year, authors, author affiliations, journals, countries, type of documents, subject area and number of citations) on male infertility and ART were collected and analysed using Scopus operational functions.

2.3 | Data retrieval strategy

The Scopus literature search, limited to human studies published from 2000 to 2019, was conducted on 28 March 2020. Selected keywords were used for each step, and in some cases followed by the asterisk '*' to include all the variants of the word. The search was performed in five steps as illustrated in Figure 1 using determined keyword strings, reported in Table S1. Once they were retrieved, the relevance of each article was evaluated by independent researchers, who screened the title and abstract of all the retrieved articles for each step. Those that were not related to the topic and animal studies were enlisted as irrelevant.

In this study, step 1 included all the literature available on 'male infertility and assisted reproductive techniques' published between 2000 and 2019. In the next steps, keywords specific for each subtopic were added to those of step 1 to obtain the relevant literature. Step 2 dealt with conventional (simple wash, double density gradient and swim up) and advanced sperm preparation techniques

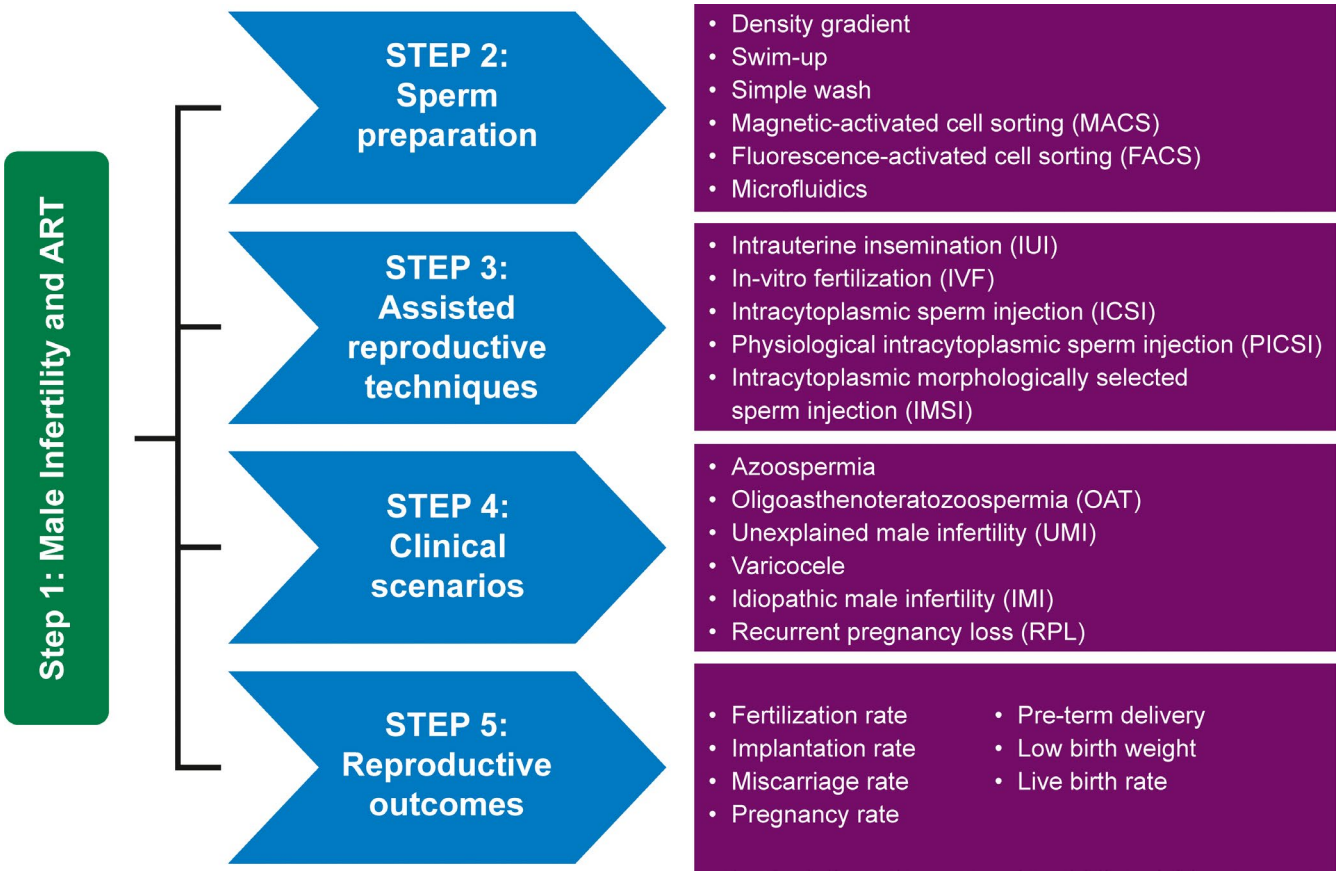

FIGURE 1 Flow diagram representing the scientometric analysis framework

(magnetic-activated cell sorting [MACS], fluorescence-activated cell sorting [FACS] and microfluidics). Step 3 analysed the techniques of assisted reproduction (IUI, IVF, ICSI, physiological intracytoplasmic sperm injection [PICSI] and intracytoplasmic morphologically selected sperm injection [IMSI]) used to overcome factors of male infertility. In step 4, we studied scientometric data corresponding to different clinical scenarios associated with male infertility and ART: azoospermia, oligoasthenoteratozoospermia (OAT), unexplained male infertility (UMI), varicocele, idiopathic male infertility (IMI) and recurrent pregnancy loss (RPL). Step 5 analysed the most frequently reported reproductive outcomes such as fertilization rate, implantation rate, miscarriage rate, pregnancy rate, pre-term delivery, low birth weight and live birth rate.

2.4 | Scientometric analyses

The scientometric data obtained were saved as comma-separated value files and subsequently converted to Microsoft Excel files for in-depth descriptive statistical analyses as previously reported (Baskaran et al., 2019). The geographic mapping based on the scientometric analysis of ART and male infertility research across the globe was obtained using Tableau Desktop (Tableau) as described in our earlier publications (Agarwal et al., 2020; Baskaran et al., 2019). A network map on international collaborations and a heat map of top scientists in male infertility and ART research were generated using VOS viewer software (downloaded from http://vosviewer.com) as detailed in our previous publications (Agarwal et al., 2020; Baskaran et al., 2019). The linear regression analysis method was utilised to investigate the publication trend in male infertility and ART research from the year 2000 to 2019.

3 | RESULTS

3.1 | Publication trends in male infertility and ART research

A scientometric analysis was conducted to analyse the publication trends on male infertility and ART research. A total of 2,148 articles were published in the last 20 years, averaging around 107 publications per year over the time period (R^2 = .041) (Figure 2). Most of the publications were original studies (n = 1,433, 66.77%) and reviews (n = 500, 23.3%), while <10% comprised conference papers, notes, editorials, short surveys, letters and book chapters. The USA had the highest number of publications (n = 511, 23.80%), followed by Italy (n = 163, 7.59%) and the United Kingdom (UK) (n = 162, 7.54%) (Figure 3). In consistent with the number of publications, the USA had more global collaborative networks between research groups (Figure 4). Furthermore, Cleveland Clinic Foundation, USA (n = 69) was

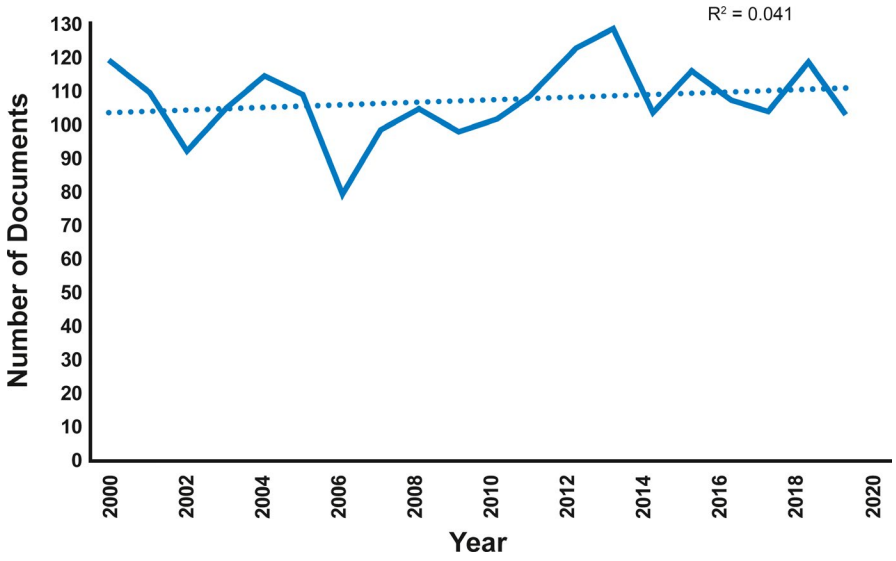

FIGURE 2 Line graph showing the number of publications per year (2000-2019) in male infertility and ART research (Step 1)

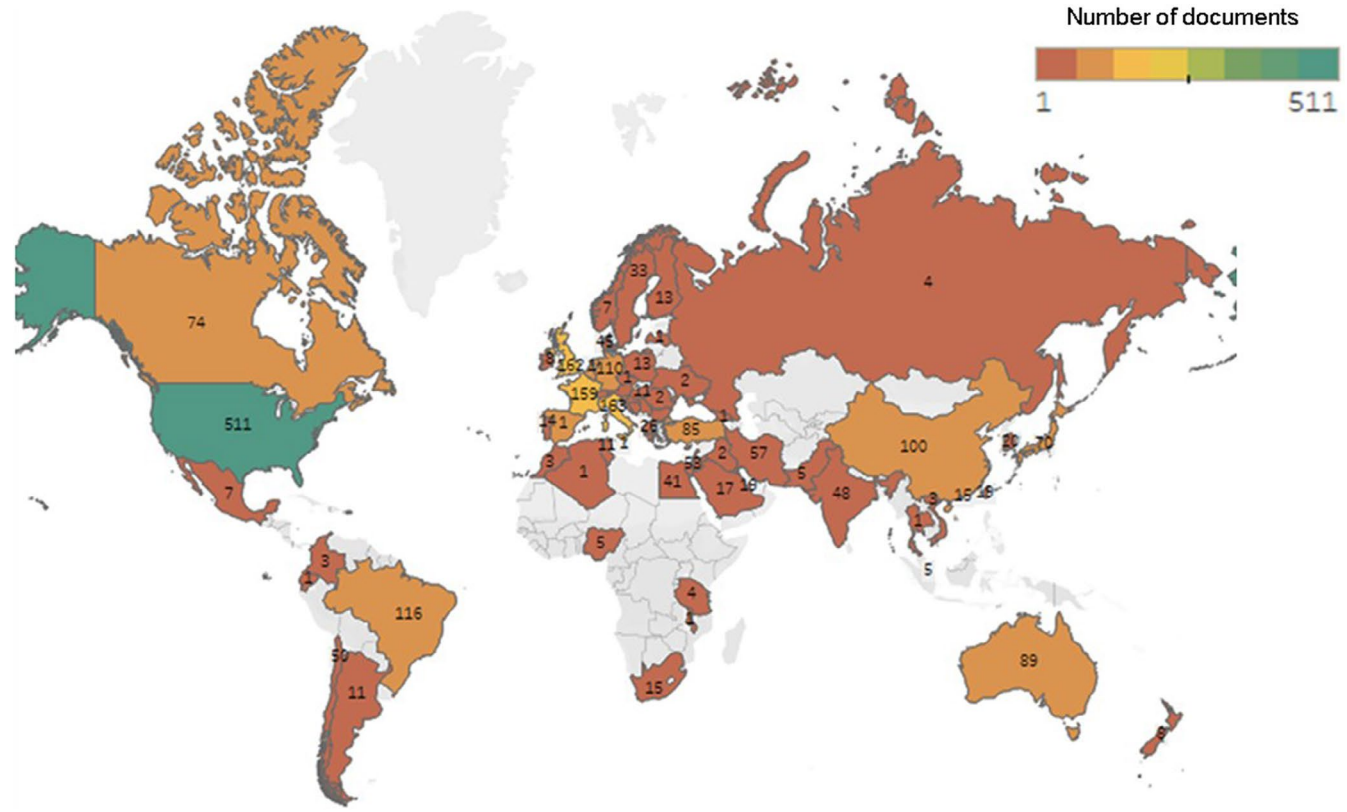

FIGURE 3 Geomap showing the distribution of publications from countries investigating male infertility and ART during the period 2000-2019

identified as the leading institution, followed by Weill Cornell Medical Center, USA ($n = 46$) and Tel Aviv University, Israel ($n = 45$) (Figure 5). Agarwal, A. was the top author publishing in this field ($n = 63$) followed by Esteves, S.C. ($n = 44$) and Tournaye, H ($n = 32$) (Figure 6). The top ten journals publishing in the area of male infertility and ART are presented in Table 1. Fertility and Sterility ($n = 228$; 10.6%), Human Reproduction ($n = 187$; 8.7%) and Reproductive Biomedicine Online ($n = 89$; 4.1%) accounted for 23% of all published studies.

3.2 | Publication trends based on sperm preparation techniques in ART

Step 2 analysed the sperm preparation techniques commonly used in the most cited ART research articles (Figure 7). The total number of publications on conventional techniques ($n = 110$) was greater than on advanced techniques ($n = 22$). Conventional techniques include density gradient centrifugation ($n = 61$), swim-up ($n = 26$) and simple

wash (n = 23), while advanced techniques include MACS (n = 11), microfluidics (n = 8) and FACS (n = 3).

3.3 | Publication trends based on different ART procedures

In step 3, we analysed the publications based on assisted reproductive procedures commonly reported (IUI, IVF, ICSI, IMSI and PICSI) in ART publications and the findings are summarised in Figure 8. The results indicate that ICSI was the most reported ART technique (n = 1,305), followed by IVF (n = 844), and IUI (n = 193), whereas IMSI (n = 52) and PICSI (n = 5) were reported less frequently. With regard to the ART techniques such as ICSI (n = 262), IVF (n = 236) and IUI (n = 57), the USA was the most productive country, followed by China (n = 111) and France (n = 97) for ICSI, the UK (n = 84) and France (n = 73) for IVF and the Netherlands (n = 26) and Canada (n = 16) for IUI (Table S2). The top three countries publishing articles on IMSI were France (n = 12), Italy (n = 8) and Austria (n = 6), while for PICSI, they were Australia, Brazil and Ecuador (n = 1 for each) (Table S2).

3.4 | Publication trend in ART and clinical scenarios

In step 4, we analysed the clinical scenarios commonly investigated in ART-related male infertility studies. Azoospermia was the most studied clinical scenario (n = 388), whereas varicocele (n = 78), OAT (n = 62), UMI (n = 47), IMI (n = 35) and RPL (n = 30) were found to be less represented in ART literature (Figure 9).

3.5 | Publication trends in reproductive outcomes associated with ART

In step 5, we analysed the publications based on the reproductive outcomes commonly reported in ART. Pregnancy rate (n = 1,134) was the most reported outcome, followed by miscarriage (n = 360), fertilization (n = 356) and implantation (n = 327) rates. A lower number of articles reported evidence about the live birth rate (n = 141), pre-term delivery (n = 41) and low birth weight (n = 41) (Figure 10).

4 | DISCUSSION

Currently, ART has an important role in the management of male factor infertility via increasing the probability of sperm fertilizing an oocyte by circumventing the functional and structural deficits of spermatozoa and the reproductive system (Tournaye, 2012). Therefore, we conducted an in-depth analysis of literature on ART and male infertility using a stepwise approach to explore the trends in publications on major domains related to ART. To the best of our knowledge, this is the first scientometric study on ART and male infertility depicting the details of publication trends on sperm preparation techniques, ART procedures, clinical scenarios and reproductive outcomes, thereby providing a deeper insight on the current status of ART in male infertility research.

It is suggested that the management of infertile men has been undoubtedly revolutionised by the advent of ICSI in clinical practice (Palermo et al., 1992) and the possibility to surgically retrieve spermatozoa directly from the testis and epididymis (Lopushnyan & Walsh, 2012). However, as a consequence, investigation into the causes of male infertility is not an indispensable requirement for the achievement of pregnancy by ART (Agarwal & Cho, 2017). This might partially explain why the publication trend on ART has not been increasing for the past two decades. It might also partially explain the steady trend instead of an increase in the number of yearly publications on ART and male infertility over the past 20 years that was noted in the current scientometric study. However, our analysis showed that 66.77% of publications were original articles, highlighting an increased research focus on the impact of andrological conditions on ART outcomes. In fact, the investigation of semen quality and andrological conditions may shed light on the additional factors influencing embryo development and live birth delivery.

In agreement with Baskaran et al. (2019), our analysis showed that the USA was the most prolific country publishing on male infertility and ART research. Generally, the western culture favours the collection of more accurate data regarding the andrological status, while religious and cultural boundaries may prevent an adequate assessment of male infertility, particularly in African or Eastern countries (Agarwal et al., 2015). Based on the most recent data provided by the UNESCO Institute for Statistics (UIS), the USA is the country with the highest amount of financing for research and development in private and public sectors worldwide, with more than 470 billion US Dollars spent every year (http://uis.unesco.org/apps/visualisations/research-and-development-spending/). Moreover, the broad network of collaboration with countries across the globe may also explain the highest number of publications on male infertility and ART research. The Cleveland Clinic Foundation and Agarwal, A. were identified as the top institution and author in the field of male infertility and ART, respectively. These findings are in agreement with previous scientometric studies on male infertility (Baskaran et al., 2019), sperm DNA fragmentation (Baskaran et al., 2019) and proteomics (Agarwal et al., 2020). Around 23% of the total publications were published in Fertility and Sterility, Human Reproduction and Reproductive Biomedicine Online, similar to findings reported previously (Baskaran et al., 2019). These journals promote excellence in the field of reproductive medicine and highly influence the current research trends on fertility, reproduction and embryo development, with each showing an impact factor of 5.411, 5.506 and 2.93, respectively.

Sperm selection is the paramount step in ART, which can be carried out by conventional or advanced techniques. While conventional techniques use the selection criteria based on sperm motility and morphology (Le Lannou & Blanchard, 1988), advanced sperm

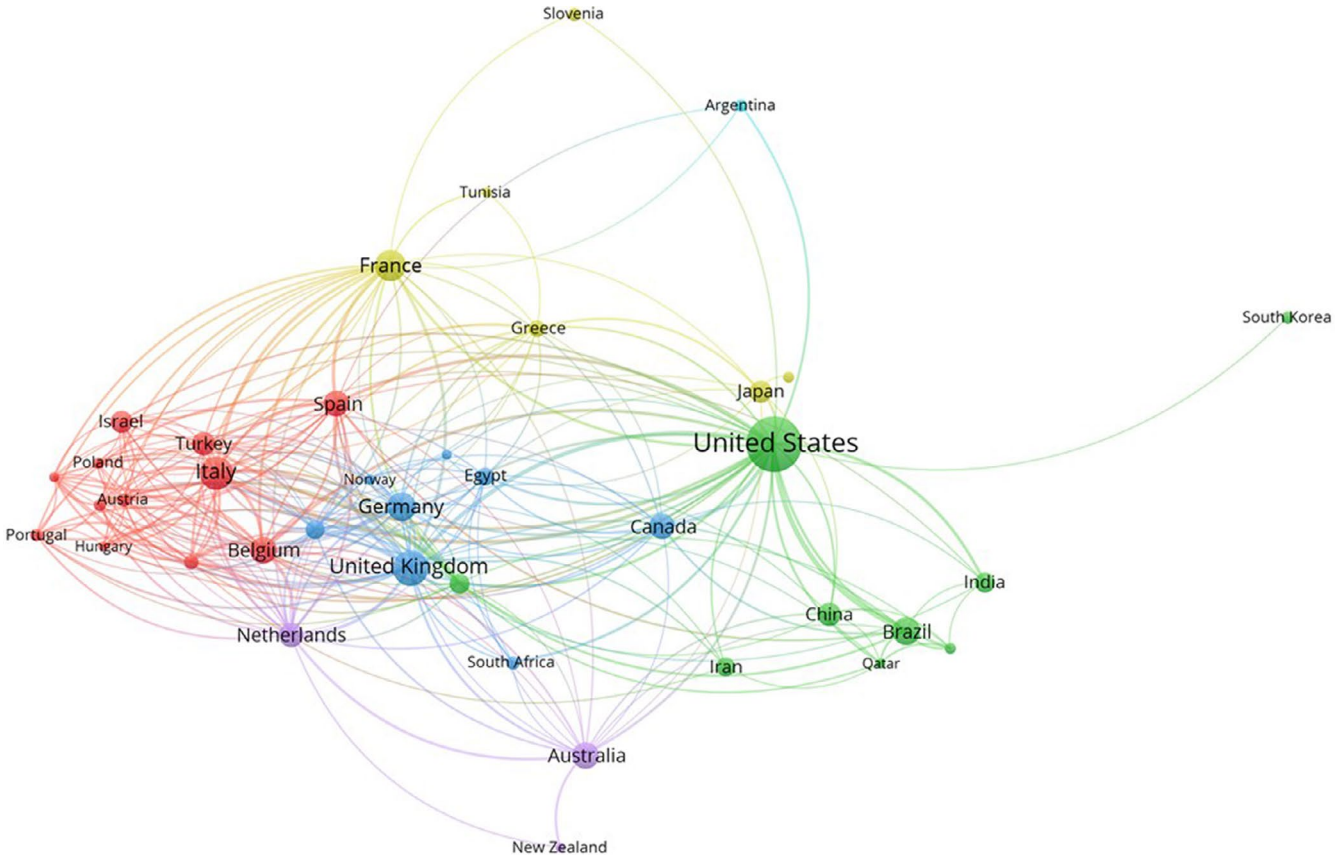

FIGURE 4 Network map reflecting international collaboration based on publications in male infertility and ART during the period 2000-2019

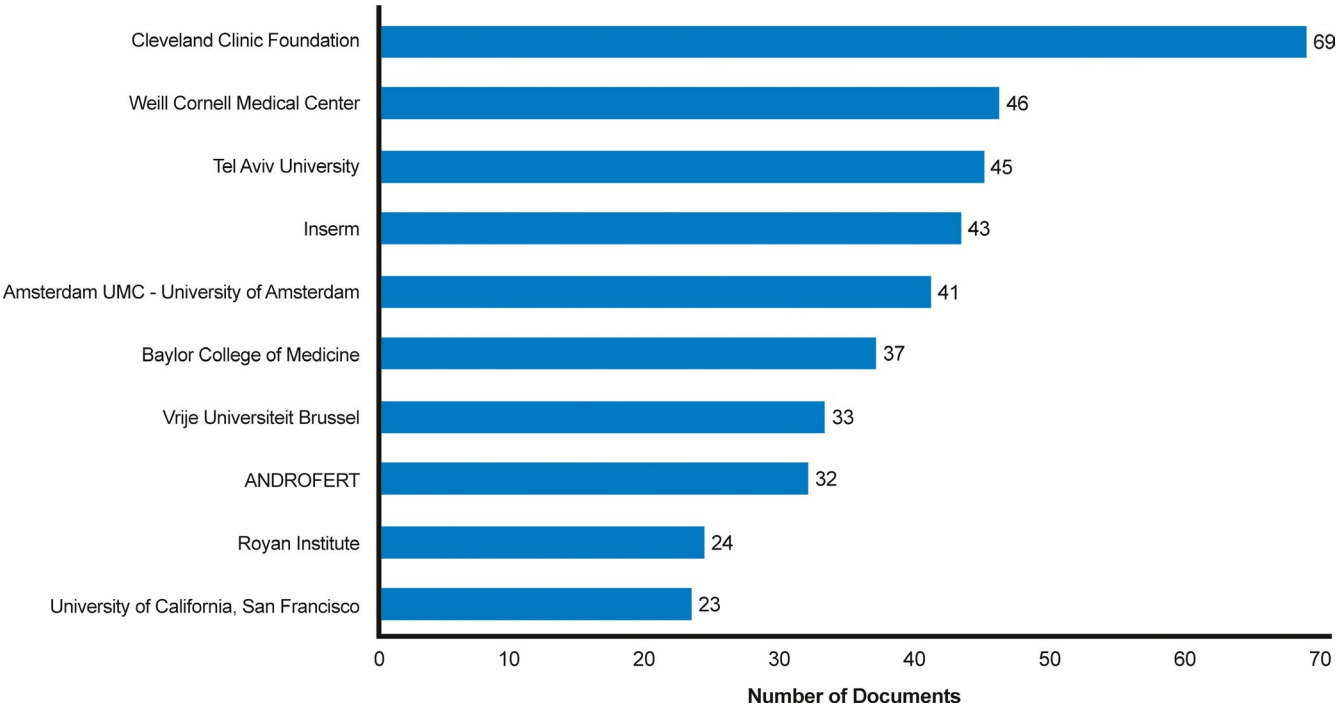

FIGURE 5 Top 10 institutions based on the total number of publications investigating male infertility and ART during the period 2000-2019

separation techniques are based on surface charge, DNA integrity, apoptosis, membrane maturity and the use of sophisticated microscopy for the evaluation of the sperm micro-structure (Said & Land, 2011). Though each technique has its advantages and disadvantages, conventional sperm preparation methods are more cost-effective and easier to handle than the available advanced techniques.

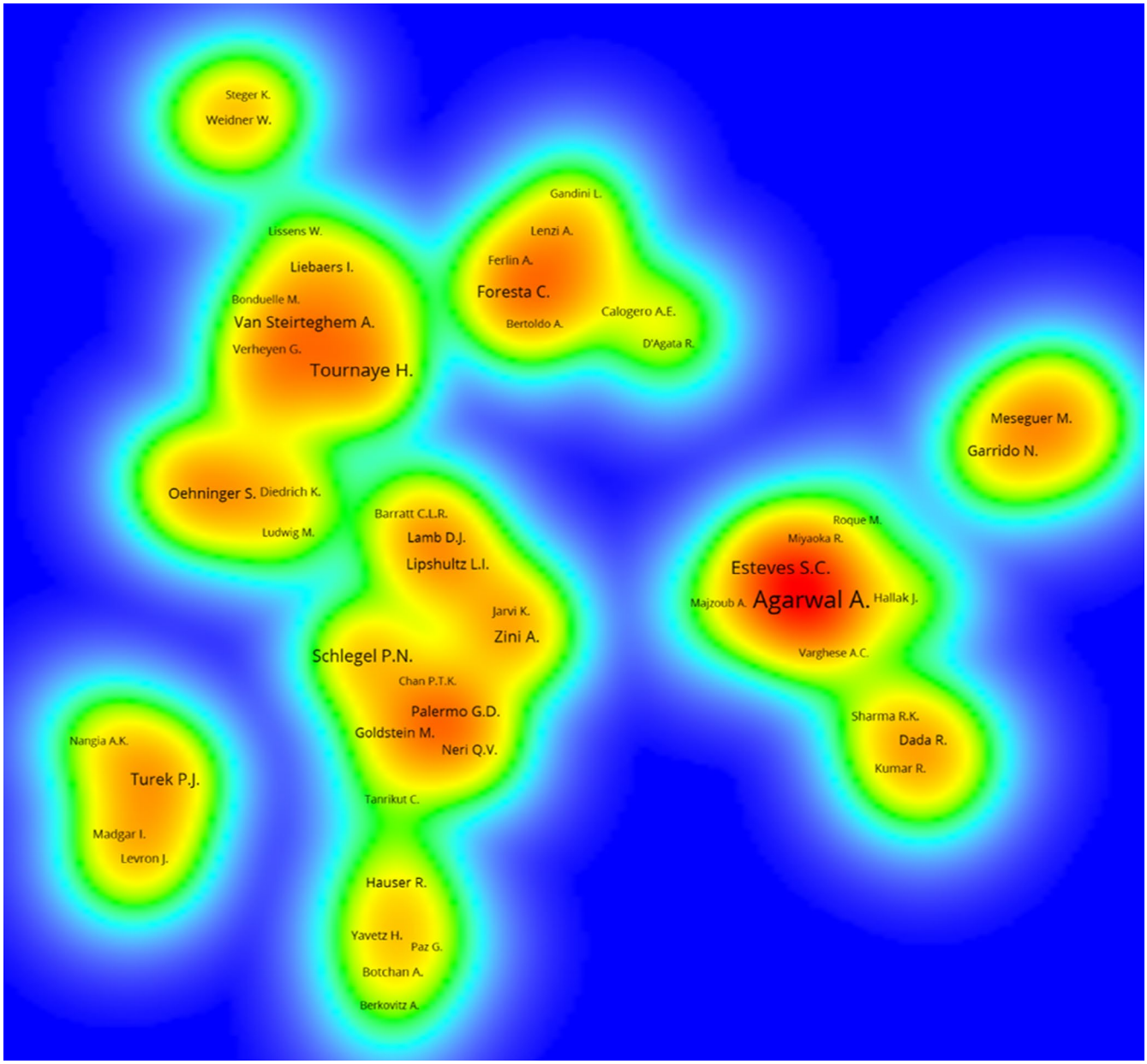

FIGURE 6 Contour/heat map showing the top authors investigating male infertility and ART (2000-2019)

Hence, they are commonly used in Andrology and IVF clinics (Henkel & Schill, 2003; Oseguera-Lopez, Ruiz-Diaz, Ramos-Ibeas, & Perez-Cerezales, 2019). This supports our current scientometric results, which reveal that the maximum number of publications on ART were based on conventional techniques.

The choice of a specific sperm preparation technique depends on the quality of the semen specimen. Density gradient centrifugation has several advantages over other conventional techniques such as the elimination of leucocytes and abnormal spermatozoa, reduction of ROS levels and a higher recovery rate than swim-up or simple wash method (Henkel & Schill, 2003). This corroborates with our results, which show that density gradient centrifugation-based sperm preparation was mostly used in ART. Despite their advantages, conventional techniques do not target the intrinsic characteristics of spermatozoa that can influence the fertilizing potential. Advanced sperm preparation techniques can overcome these shortcomings by selecting the best sperm for ICSI and IVF.

The MACS technique is able to select sperm with high DNA integrity and oocyte penetration capacity (Zahedi et al., 2013), and significantly improve the pregnancy rate in infertile patients (Dirican et al., 2008; Ziarati, Tavalaee, Bahadorani, & Nasr Esfahani, 2019). Despite its advantages, MACS is yet to be certified by the Food and Drug Administration, especially with regard to the safety pertaining to the use of micro-magnetic beads (Plouffe, Murthy, & Lewis, 2015), thus limiting its use in ART procedures. The major drawback of the FACS technique is the cost of the equipment and requirement of technically skilled persons to use the instrument (Plouffe et al., 2015). New devices based on microfluidics can select sperm with high DNA

TABLE 1 The top 10 journals publishing research on male infertility and ART during the period 2000-2019 (Step 1)

Rank	Journal name	# of publications
1	Fertility and Sterility	228
2	Human Reproduction	187
3	Reproductive Biomedicine Online	89
4	Journal of Assisted Reproduction and Genetics	86
5	Andrologia	75
6	Asian Journal of Andrology	67
7	Translational Andrology and Urology	35
8	Journal of Urology	35
9	Andrology	34
10	Human Reproduction Update	28

integrity (Kishi et al., 2015; Nosrati et al., 2014; Quinn et al., 2018), which is considered a good predictor of IVF and ICSI outcomes (Jin et al., 2015; Osman, Alsomait, Seshadri, El-Toukhy, & Khalaf, 2015). Our scientometric analysis also revealed that a maximum number of publications in 2019 was based on microfluidic technique when compared to other advanced sperm selection techniques. Since the first clinical trial using microfluidics sperm selection was conducted in 2019 (Yetkinel et al., 2019), the generation of more data related to the clinical outcomes of microfluidics may potentially increase its usage in the future.

IVF and ICSI have dominated the ART landscape in male infertility at the expense of other less invasive techniques such as IUI. However, IUI is still the first-line of treatment in cases of isolated cervical factor, unexplained couple infertility, or sexual disorders (Ombelet, 2013). Although IVF revolutionised infertility treatment, poor semen quality remains associated with poor outcomes in IVF (Stephens et al., 2013). ICSI involves the injection of a single spermatozoon into the oocyte; thus, it represents the gold standard technique in case of cryptozoospermia (Palermo et al., 1992, 2017), whereas in IVF, a minimum seminal concentration of 200,000 motile spermatozoa/mL is required for fertilization (Speyer et al., 2019). ICSI has been successfully applied to overcome severe male factor infertility presentations, including oligozoospermia, asthenozoospermia and teratozoospermia, or a combination of these, as well as in case of recurrent IVF failures (Palermo, Neri, Schlegel, & Rosenwaks, 2014; Speyer et al., 2019). Furthermore, ICSI bypasses sperm kinetic defects, the presence of anti-sperm antibodies, acrosome dysfunction and the lack of maturity in gametes collected directly from the epididymis or testicles (Palermo et al., 2014). These findings might explain the dominant research focus on ICSI (Avalos-Duran et al., 2018; Palermo et al., 2014, 2017).

IMSI and PICSI are advanced ICSI-related techniques that are poorly studied (Avalos-Duran et al., 2018; Teixeira et al., 2020), as reflected in our scientometric results. IMSI is characterised by sperm selection based on morphological criteria under a high-resolution microscope (Kim et al., 2014; Oseguera-Lopez et al., 2019), whereas in PICSI, spermatozoa are selected using hyaluronic acid binding to mature and morphologically intact spermatozoa (Avalos-Duran et al., 2018). PICSI and IMSI have not shown many benefits in reproductive outcomes over conventional ICSI, including fertilization, implantation, clinical pregnancy, miscarriages and live birth rates, as well as embryo quality (Avalos-Duran et al., 2018; Teixeira et al., 2020). Importantly, some studies suggest a benefit of sperm DNA quality using these techniques, whereas others have failed to demonstrate any additional advantage (Bradley et al., 2016; Esteves, Roque, Bradley, & Garrido, 2017; Kim et al., 2014). Studies reporting benefits in using IMSI or PICSI instead of ICSI currently lack strong

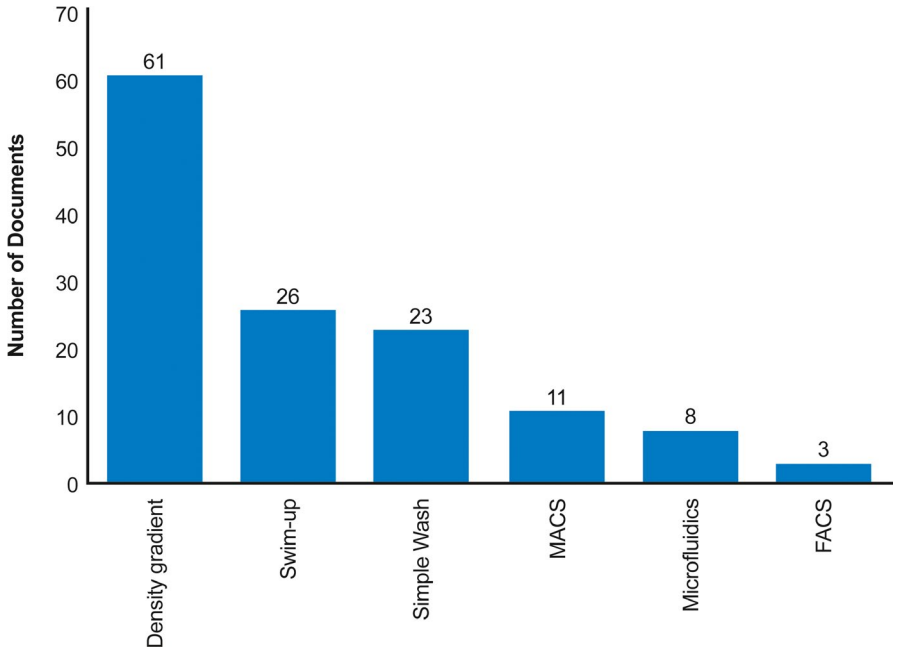

FIGURE 7 Publications investigating male infertility and ART using different sperm preparation techniques during the period 2000-2019 (Step 2)

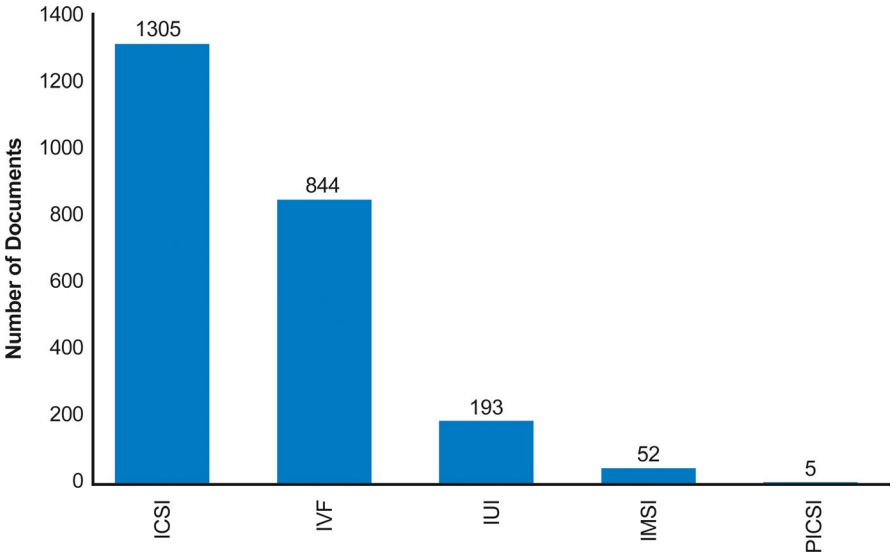

FIGURE 8 Publications investigating male infertility and ART using different ART techniques during the period 2000-2019 (Step 3)

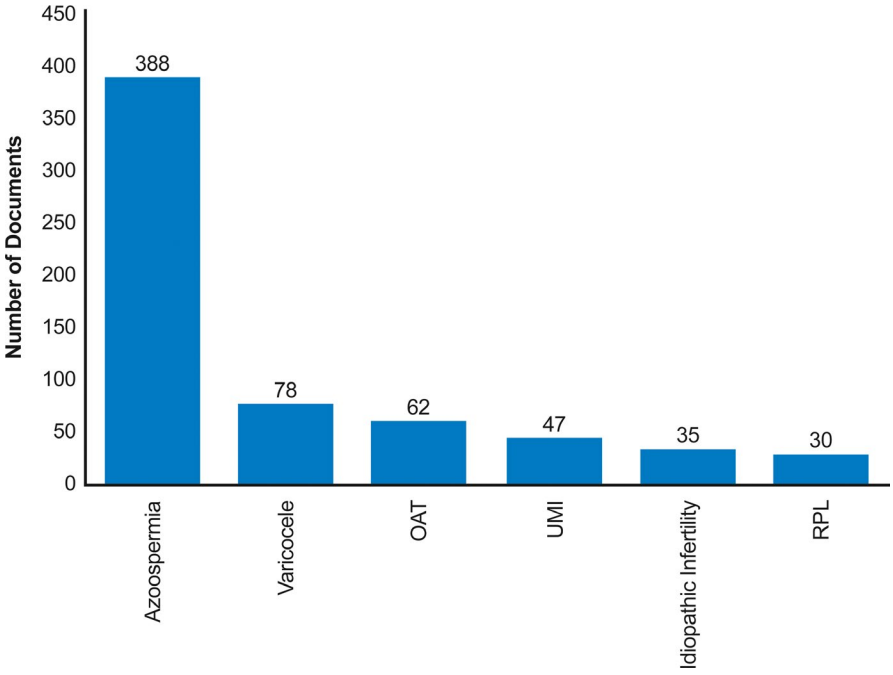

FIGURE 9 Publications on male infertility and ART investigating different clinical scenarios during the period 2000-2019 (Step 4)

evidence and may be due to the existence of only a few studies using IMSI or PICSI. Therefore, further investigations remain recommended (Avalos-Duran et al., 2018; Teixeira et al., 2020).

Several clinical conditions related to male infertility can be overcome by ART. Azoospermia is classified as obstructive (OA), when there is occlusion of the ductal system, or nonobstructive (NOA), when there is a lack of spermatogenesis (Esteves, 2015; Zegers-Hochschild et al., 2017). Although not considered a diagnosis, azoospermia is present in 15% of infertile males and 1% of the total male population (Esteves, 2015). OA can be managed through surgical interventions to repair occlusions, or ICSI via sperm retrieval from the testis or the epididymis (Practice Committee of the American Society for Reproductive Medicine in collaboration with the Society for Male Reproduction & Urology, 2019), whereas sperm retrieval for ICSI is a common treatment option for NOA (Esteves, 2015). The majority of NOA males has spermatogenic failure, where 30%-60% of patients have viable spermatozoa on biopsy and rely on ICSI (Esteves, 2015). In contrast to these limited options, patients diagnosed with varicocele, OAT, IMI, UMI and RPL have a broader spectrum of treatments that can be employed before ART (Agarwal et al., 2019; Duca, Calogero, Cannarella, Condorelli, & La Vignera, 2019; Hamada, Esteves, Nizza, & Agarwal, 2012). This may explain the disproportionate focus on azoospermia compared to other causes of male infertility.

Varicocele is diagnosed in up to 40% of infertile males and found in 15% of the male population (Johnson & Sandlow, 2017). Although it is a prominent cause of infertility, varicocele was found to be the second most common clinical scenario studied in the context of ART and male infertility. This may be due to varicocele being considered as the leading cause of correctable male infertility, particularly through

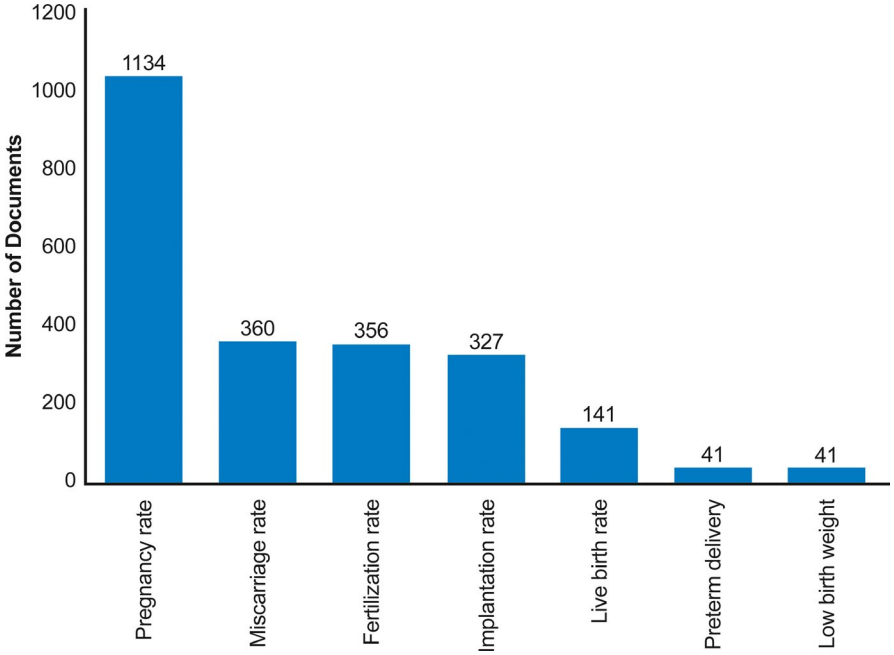

FIGURE 10 Publications on male infertility and ART investigating different ART outcomes during the period 2000-2019 (Step 5)

varicocelectomy (Johnson & Sandlow, 2017; Lundy & Sabanegh Jr, 2018), which reduces the need for ART from 54% to 38% (Cayan & Akbay, 2018; Samplaski, Lo, Grober, Zini, & Jarvi, 2017; Zini, Boman, Baazeem, Jarvi, & Libman, 2008). This may explain the significantly less research focus on this common clinical presentation, although it did receive significant attention.

Similarly, OAT, IMI and UMI may have numerous treatment options, reflecting the reduced research focus on these presentations in ART. Although ART interventions remain the main option in these patients, hormonal, antioxidant, lifestyle and surgical interventions may be considered as well (Agarwal et al., 2019; Colpi et al., 2018; Duca et al., 2019; Hamada, Esteves, & Agarwal, 2011). RPL, defined as two or more failed clinical pregnancies (Robinson et al., 2012), was studied in only 4.6% of the retrieved articles. Despite adequate investigation, 50% of the cases are considered as idiopathic (Practice Committee of the American Society for Reproductive Medicine, 2012). Several authors have described an association between male factor and RPL (Kavitha & Malini, 2014; Ramasamy et al., 2015; Zidi-Jrah et al., 2016); in contrast, other authors reported no association between RPL and semen parameters (Carlini et al., 2017; Eisenberg, Sapra, Kim, Chen, & Buck Louis, 2017). The lack of good quality data establishing a relationship between male infertility and RPL is a possible explanation for the decreased interest in this clinical scenario.

In an ART setting, several parameters are used to describe the reproductive outcomes. In this study, reproductive outcomes such as fertilization, implantation, miscarriage, pregnancy and live birth rates as well as pre-term delivery and low birth weight were included, as they mostly describe all the steps involved in the reproductive process. Scientometric analysis revealed the highest number of publications for pregnancy rate, followed by miscarriage and fertilization rates. According to the WHO, fertility is defined as "the capacity to establish a pregnancy" (Zegers-Hochschild et al., 2017). Hence, majority of the studies related to male infertility and ART considered pregnancy rate as the most suitable reproductive outcome. Furthermore, sperm quality and DNA fragmentation, which are considered as main factors of male factor infertility, are significantly associated with reduced fertilization and pregnancy rates and increased miscarriage rate (Benchaib et al., 2003; Robinson et al., 2012; Xue et al., 2016). This may explain why these outcomes have been mainly investigated in the literature.

According to our results, reproductive outcomes such as live birth rate, pre-term delivery and low birth weight were found to be less investigated. The ultimate goal or success of the ART technique depends on the birth of a healthy offspring. Live birth rate is defined as "the number of deliveries that resulted in at least one live birth, expressed per 100 cycle attempts" (Zegers-Hochschild et al., 2017), and it is adjusted for miscarriages and stillbirths, which may also be related to multiple maternal and foetal factors. In fact, once a clinical pregnancy is established, several factors such as the exposure to environmental toxins, chromosomal as well as congenital anatomic abnormalities, infections, hormonal and lifestyle factors, and chronic diseases can result in pregnancy loss (Ha et al., 2018; Practice Committee of the American Society for Reproductive Medicine, 2012). Therefore, the live birth rate (and not pregnancy rate) should be considered as the final reproductive outcome. A relatively lesser number of publications based on live birth rate may be due to the fact that most of the ART centres mainly focus until a pregnancy is achieved, but neglect the further medical follow-up. Moreover, some patients travel abroad, especially to developed countries, to have access to more specialised ART treatments which are limited in their home countries due to legislative restrictions or lack of appropriate reproductive medicine expertise (Präg & Mills, 2017; Shenfield et al., 2010). The majority of these patients travel back to their home countries after they have conceived, and hence, the follow-up on the live birth rate outcome is not possible in these patients.

Pre-term delivery is defined as a birth of offspring within 39 weeks of gestation, which contribute to nearly 10% of all births (Howson, Kinney, McDougall, & Lawn, 2013). This condition is one of the main causes of child mortality (Howson et al., 2013) and has been recently associated with the development of neurological problems (Ream & Lehwald, 2018) as well as a higher risk of cardiovascular and renal complications (Chehade, Simeoni, Guignard, & Boubred, 2018). Basso and Baird reported that the risk of adverse birth outcomes is high in infertile women, regardless of the ART techniques applied (Basso & Baird, 2003). Evidence also suggests a correlation between low birth weight and risk of cancer, overweight and diabetes (Eriksen, 2014). Nevertheless, our scientometric analysis revealed very few publications related to pre-term delivery and low birth weight outcomes, whereas more importance was given to pregnancy rate. Therefore, further research is clearly warranted for a better understanding of the relationship between male infertility and late reproductive outcomes such as live birth rate, pre-term delivery and birth weight.

Like any other study, this work is not free of limitations. Although keywords were used to retrieve maximum number of relevant articles on male infertility and ART, the articles that are not indexed in Scopus were not included in the scientometric analysis.

5 | CONCLUSIONS

In conclusion, our analysis revealed a stable trend in the publications related to male infertility and ART in the last two decades. ART research is mainly focused on azoospermic condition while the ICSI technique is widely used for the treatment of male factor infertility. Currently, a substantial increase in the number of clinical studies evaluating late reproductive outcomes, such as live birth rate, pre-term delivery and birth weight, is required to determine the actual success of ART procedures recommended for male factor infertility.

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CONFLICT OF INTEREST

None of the authors have any conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

A.A. involved in conceptualisation, supervision, investigation and project administration. A.A., M.K.P.S., K.L., R.F., C.B., P.N.P., K.A.R., R.A., C.I., D.D., S.B. and R.H. involved in formal analysis. M.K.P.S., K.L., R.F., C.B., P.N.P., D.D. and S.B. involved in data curation. M.K.P.S., S.B. and R.H. involved in methodology. M.K.P.S., R.F. and P.N.P. involved in software. M.K.P.S.and S.B. involved in validation. M.K.P.S., K.L., R.F., C.B., P.N.P., K.A.R., R.A., C.I., D.D., S.B. and R.H. involved in writing-original draft preparation. M.K.P.S., K.L., R.F., C.B., P.N.P., K.A.R., R.A., C.I., D.D., S.B. and R.H. involved in writing-review and editing. All authors read and agreed to the published version of the manuscript.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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