


CLINICAL ARTICLE

Gynecology

Ten years of in vitro fertilization in Indonesia: Access to infertility care in a developing country

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Abstract

Objective: This research was conducted to assess access to assisted reproductive technologies (ART) and the current status of the in vitro fertilization (IVF) program that have been implemented in Indonesia over the last 10 years.

Methods: We established a retrospective cohort study and descriptive analysis of the current state of access to infertility care in Indonesia. The data were collected from all IVF centers, clinics, and hospitals in Indonesia from 2011 to 2020, including the number of IVF clinics, total ART cycles, retrieved fresh and frozen embryos, average age of IVF patients, IVF pregnancy rate, and causes of infertility.

Results: The number of reported fertility clinics in Indonesia has increased from 14 clinics in 2011 to 41 clinics by 2020. As many as 69 569 ART cycles were conducted over the past 10 years, of which 51 892 cycles used fresh embryos and 17 677 cycles used frozen embryos. The leading cause of consecutive infertility diagnosis was male infertility. Nearly half of the women who underwent IVF procedures (48.9%) were under 35 years old. The pregnancy rate outcome of women who underwent IVF ranged from 24.6% to 37.3%.

Conclusion: Developments in ART in Indonesia have led to improvements in the ART cycles performed throughout the 10 year period. The identification of key areas that require improvement can provide an opportunity to enhance access to infertility care.

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assisted reproductive technology, female infertility, fertility clinics, in vitro fertilization, Indonesia, infertility, infertility care, male infertility

1 | INTRODUCTION

Infertility is a global public health concern that affects millions of people of reproductive age. The global rate of infertility varies in every country and region, with the prevalence estimated to be increasing by 3.5% to 16.7% in developed countries, whereas in developing countries, it ranged from 6.9% to 9.3%.¹ The prevalence of infertility increased in some areas as it appears up to 30% of sub-Saharan Africa couples are infertile.²

Considering new technological advances in infertility treatment, much research has been developed to improve the success of infertility management and the outcome of in vitro fertilization (IVF). However, in resource-limited settings, the utilization of assisted reproductive technologies (ART) research was limited. Although being available for nearly three decades, assisted reproduction is inaccessible to most of the citizens of resource-poor countries.^{3,4} Insufficient resources and overpopulation are two commonly used arguments for this condition, therefore infertility care remains a neglected priority for health care providers in low- and middle-income countries.⁴

Indonesia as a developing country poses quite a challenge in the implementation of IVF. Infertility is one of the many major health issues in Indonesia, and as ART is quite a challenge to most, it is critical to have adequate access to advanced treatment such as IVF.⁵ It is also known that lack of reproductive knowledge, information sources and education about infertility contributes to inadequate access to IVF treatment.^{5,6} Therefore, it is important to address the needs of low-income infertile couples, particularly those living in developing countries with different variations of economical background, to get access to adequate infertility care.

The Indonesian national regulation on ART use stated that IVF treatment can only be done in husband and wife who had infertility

in either one or both, using their own sperm and ovum and the fertilized egg can only be implanted in the woman's womb from which the ovum originates. Furthermore, the use of genetic material donor (such as sperm, oocytes, zygotes) for reproduction purposes is prohibited for social, religious, and ethical reasons. Although this regulation may affect the number of IVF cycles performed as it prohibits ART use in otherwise fertile couples and the use of donor, this ensures that there is a certainty regarding parents of the child resulting from IVF.^{7,8}

To date, there is little known about infertility care and management in Indonesia. The purpose of this study was to assess access to ART and the current status of the IVF program that have been implemented in Indonesia over the last 10 years. We present a descriptive data of the current status of the IVF program that has been implemented in Indonesia over the last 10 years.

2 | MATERIALS AND METHODS

We established a retrospective cohort study based on collected IVF data in Indonesia. The data obtained was the previous years' data from all IVF centers, clinics, and hospitals in Indonesia over the last 10 years (2011–2020). Ethics approval was not obtained as this study used statistical data about IVF and no personal data of the patients was used. Informed consent was obtained by each clinic prior to the IVF procedure. The reported data were the number of IVF clinics, total ART cycles, retrieved embryos and embryos frozen, age of IVF patients, IVF pregnancy rate, and causes of infertility. The diagnosis of pregnancy was made clinically, which is when there is a presence of gestational sac in the uterus through ultrasound examination. All of the data collected from each clinic were validated by the Indonesian Association for In Vitro Fertilization (IA-IVF). The data were represented by its

descriptive data, obtained through SPSS version 26 (IBM, Armonk, NY, USA) and shown by graphics and diagrams.

3 | RESULTS

The number of reported fertility clinics in Indonesia has constantly risen over the last 10 years (seen in Table 1). In 2011, Indonesia had

14 fertility clinics, and its numbers have progressively increased until 2020 to 41 fertility clinics spread throughout Indonesia. To date, the number of fertility clinics in Indonesia has reached 56. A total of 69 569 ART cycles were conducted over the past 10 years, of which 51 892 (74.6%) cycles used fresh embryos and 17 677 (25.4%) cycles used frozen embryos (see Figure 1). The average ART cycle annually was 6956 cycles, while the average fresh embryos and frozen embryos retrieved each year were 5189 and 1767 embryos,

TABLE 1 Total in vitro fertilization program in Indonesia 2011–2020.

Variable	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
Reporting clinic	14	21	22	27	26	28	32	34	38	41	41
Total assisted reproductive technologies cycles	2627	3581	4083	4877	6008	7699	9122	10433	12140	8999	69569
Fresh embryo	2282	3154	3488	4127	4991	6092	6648	7271	8112	5727	51892
Frozen embryo	345	427	595	750	1017	1607	2474	3162	4028	3272	17677

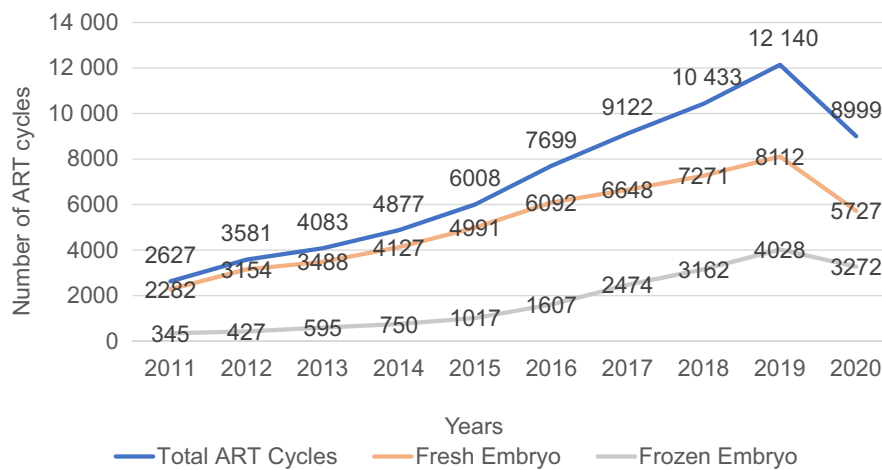


FIGURE 1 Total assisted reproductive reproductive technologies (ART) cycles in Indonesia in 2011–2020.

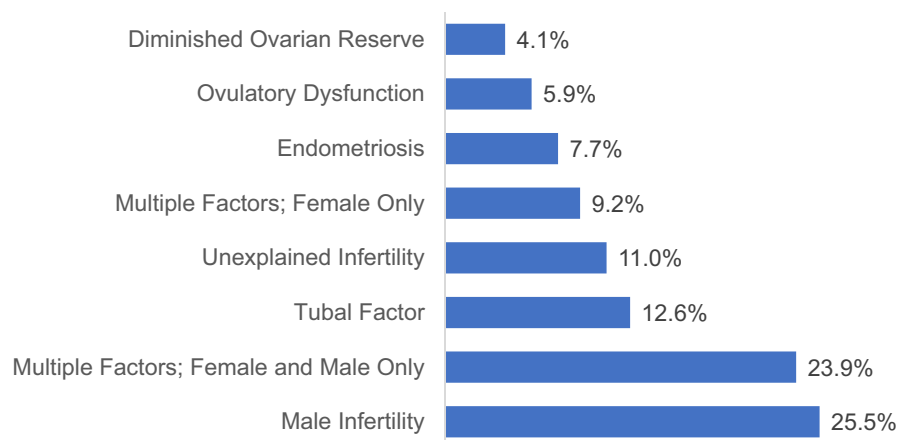


FIGURE 2 Causes of infertility.

respectively. There was an increasing trend in the annual total ART cycles from 227 in 2011 to 12 140 in 2019; however, a decrease was shown in 2020 to 8999 cycles (Table 1).

The main diagnosis of causes were male infertility (25.5%), multiple factors (female and male only) (23.9%), tubal factor (12.6%), unexplained infertility (11.0%), multiple factors (female only) (9.2%), endometriosis (7.7%), ovulatory dysfunction (5.9%), and diminished ovarian reserve (4.1%) (seen in Figure 2). Male factor has consistently been the most common cause of infertility from 2011 until 2017. The most common cause of infertility in 2018 until 2020 were multiple factors affecting husband and wife, with male infertility as the second most common cause, while the remainder are contributed by tubal factors, ovulatory dysfunction, diminished ovarian reserve, endometriosis, female multiple factors, and unexplained infertility.

The definition of multiple factors in the “female only” category is patients with more than one diagnosis contributing to infertility. On the other hand, “multiple factors” in both female and male signifies patients who had more than one diagnosis for each partner.

In accordance with the proportion of women who underwent the IVF procedure, almost half of them (48.9%) were aged under 35 years old. The pregnancy rate of women regardless of age who underwent IVF ranged between 24.6% to 37.3% (seen in Table 2; Figure 3), with an overall decreasing trend observed from 2011 to 2016, which was increased in 2017–2018 before proceeding with another decrease throughout 2019 to 2020. As seen in Figure 3 and Table 3, both age groups had similar decreasing trend throughout the period although women ≥35 years old generally had lower pregnancy rate compared to those aged <35 years old.

4 | DISCUSSION

In this study, the increase which began in 2011 from 14 to 41 clinics in 2020 spread throughout Indonesia with supervision from the Ministry of Health. IVF services are spread across Medan, Palembang, Padang, Jakarta, Bandung, Surakarta, Semarang, Magelang, Yogyakarta, Pontianak, Makassar, Surabaya, and Bali. Based on the Central Agency on Statistics Indonesia data in 2021, Indonesia consists of 16 766 islands with a total area of 1 916 906.77 km².⁹ There are five main islands in Indonesia; Sumatra island, Java island, Kalimantan island, Sulawesi island, and Papua island. Until 2020, most of the Indonesia IVF clinics were located in Java island (32 clinics from 41 clinics). Java island is the most population-dense island in Indonesia, consisting of more than half of the Indonesian population in 2020.¹⁰ Java island is the island where the Indonesian capital city is located, and therefore it is considered to be the most developed Island in Indonesia.⁹ Until 2020, IVF clinics were unavailable in most Indonesian locations. On Kalimantan island, which is around 539 460 km², one IVF clinic is located in West Kalimantan, Pontianak. Sulawesi island has a total area around 189 216 km² but there are only two IVF clinics, located in Makassar, South Sulawesi. There are no IVF clinics on Papua island, Maluku island, and Nusa Tenggara island.⁹ This becomes one of the barriers

TABLE 2 Characteristics of in vitro fertilization patients in Indonesia (2011–2020).

Total n (%)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Average
<35 years old	1216 (46.3)	1795 (50.1)	1907 (48.0)	2354 (48.3)	2935 (48.9)	3773 (49.0)	4262 (49.4)	4700 (49.6)	5408 (48.4)	4169 (50.1)	3252 (48.9)
≥35 years old	1357 (51.7)	1786 (49.9)	2063 (52.0)	2523 (51.7)	3073 (51.2)	3926 (51.0)	4373 (50.6)	4781 (50.4)	5766 (51.6)	4157 (49.9)	3381 (51.0)
35–37 years old	595 (22.7)	735 (20.5)	844 (21.3)	1088 (22.3)	1291 (21.5)	1678 (21.8)	1814 (21.0)	2019 (21.3)	2993 (21.4)	1711 (20.6)	1417 (21.4)
38–40 years old	460 (17.5)	627 (17.5)	704 (17.7)	826 (16.9)	992 (16.5)	1272 (16.5)	1415 (16.4)	1575 (16.6)	1850 (16.6)	1379 (16.6)	1110 (16.9)
41–42 years old	194 (7.4)	258 (7.2)	303 (7.6)	348 (7.1)	417 (6.9)	528 (6.9)	627 (7.3)	620 (6.5)	748 (6.7)	542 (6.5)	459 (7.0)
>42 years old	108 (4.1)	166 (4.6)	212 (5.3)	261 (5.4)	373 (6.2)	448 (5.8)	517 (6.0)	567 (6.0)	775 (6.9)	525 (6.3)	395 (5.7)

for infertility services in Indonesia, which is supported by the studies of Halim et al. and Bennett et al. They found that the geographical barrier significantly correlated with the access barrier in Indonesia infertility services.^{11,12} Geographical factor as an infertility services barrier was also supported by the Brodeur et al. and Mackay et al. studies.^{13,14} Geographical aspect becomes an infertility services barrier due to more time and more money that patients must spend for this service, and thus more inconvenience and social-psychological burden for the patients.^{12,14}

Most of the treatment cycles, however, were performed in centers located in larger metropolitan cities. The disparity in the number of cycles performed in metropolitan cities compared to other areas in Indonesia can be attributed to the relatively high costs of IVF, fear of infertility diagnosis and its social burden, and lack of a proper referral system regarding the use of IVF.¹² Lack of access to IVF services has also been shown in other developing countries such as Thailand.¹⁵ Harzif et al. and Halim et al. in their studies found that in Indonesia the economic status and sociocultural factor are becoming access barriers for infertility services in urban area.^{5,11} Studies by Brodeur et al. and Mackay et al. also showed that socioeconomic and ethnic factors as infertility services access barriers.^{13,14} IVF policy in Indonesia is different from other countries, in which the Indonesian legal policy prohibits gamete donor, surrogacy, and gestational carrier.^{8,16} This could encourage Indonesian people to seek IVF procedures in other countries in order to undertake the methods that are prohibited in Indonesia. Cross-border reproductive care (CBRC) due to infertility treatment legal issue in other country is also supported by the findings of Simopoulou et al. and Salama et al.^{17,18} Furthermore, IVF clinics are still not distributed completely in all of the regions of Indonesia, which could also encourage Indonesian people to undertake CBRC.

IVF cycles continued to grow pre-pandemic and despite the challenging period, there were still a remarkable number of treatment cycle numbers performed in 2020 (8999 cycles). During the period of COVID-19 pandemic, the IVF clinics in Indonesia limited the opening time to minimize exposure and transmission of the SARS-CoV-2 virus, as infection may potentially affect the pregnancy. Patients who are going to have the embryo transfer

performed may schedule the appointment after discussion with the clinician for the appropriate time. The relationship between COVID-19 and its effects on pregnancy was supported by the findings of studies conducted by Wei et al., who found that COVID-19 is associated with pre-eclampsia, gestational diabetes, preterm birth, stillbirth, and low birth weight.¹⁹ A total of 2851 (49.8%) out of 5727 initiated fresh embryo cycles were canceled, and frozen embryo cycles comprised 3272 (36.3%) of 8999 cycles. This similar trend is seen elsewhere where utilization of frozen transfer is increasingly favored.²⁰

From 2019 to 2020, there was a decrease in total ART cycles in Indonesia. This finding is consistent with the findings of the Rashidi et al. study, which compares the cause of ART cycle canceling before and during COVID-19 and showed significantly different results. In the Rashidi et al. study, canceling the ART cycle was probably because of fear and patients being unaware about COVID-19.²¹ The pregnancy rate between 2019 and 2020 in Indonesia also decreased; however, some studies such as those conducted by Rashidi et al. and Hu et al. study show that COVID-19 did not affect the clinical pregnancy rate.^{21,22}

It is encouraging that in 2020, 85.9% of IV pregnancies were singleton, 12.9% were twins, and 1.2% were triplets. Unfortunately, currently there is no national registry of ART births in Indonesia. Therefore, it is very difficult to obtain live birth rates as one of the most important outcomes in ART.

Both fresh and frozen embryos are used in IVF practice. Embryos are frozen because of the limitation on the number of embryos transferred into the uterus: excess embryos can be stored for transfer at another time without having to repeat the ovarian stimulation, oocyte retrieval, fertilization, and the incubation process. Freezing is also carried out in patients who are threatened with loss of reproductive function such as patients with endometriosis and Turner's syndrome.²³

The overall success of human reproduction, either naturally or using the IVF method, is highly dependent on maternal age. In our data, it can be seen that women younger than 35 years old generally had higher pregnancy rates throughout the 10 years when compared to those 35 years old and above. The main reasons for age-related infertility include reduced ovarian reserve and decreased oocyte/

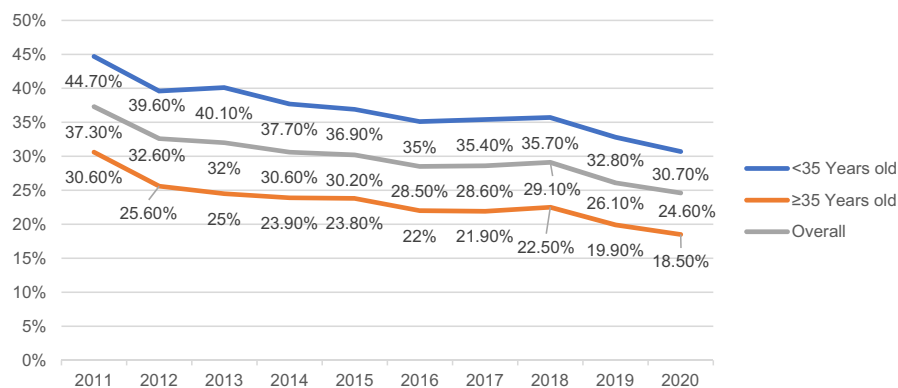


FIGURE 3 In vitro fertilization pregnancy rate in Indonesia in 2011–2020.

TABLE 3 In vitro fertilization cycles resulting in pregnancy.

Total n (%)	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Average
Overall	959 (37.3)	1168 (32.6)	1271 (32.0)	1490 (30.6)	1813 (30.2)	2191 (28.5)	2467 (28.6)	2754 (29.1)	2918 (26.1)	2048 (24.6)	1907 (29.9)
<35 years old	544 (44.7)	711 (39.6)	765 (40.1)	887 (37.7)	1083 (36.9)	1326 (35.1)	1508 (35.4)	1679 (35.7)	1773 (32.8)	1280 (30.7)	1156 (36.9)
≥35 years old	415 (30.6)	457 (25.6)	506 (24.5)	603 (23.9)	730 (23.8)	865 (22.0)	959 (21.9)	1075 (22.5)	1145 (19.9)	768 (18.5)	752 (23.3)
35–37 years old	243 (40.8)	233 (31.7)	271 (32.1)	316 (29.0)	413 (32.0)	487 (29.0)	519 (28.6)	609 (30.2)	618 (25.8)	396 (23.1)	411 (30.2)
38–40 years old	128 (27.8)	166 (26.5)	176 (25.0)	199 (24.1)	231 (23.3)	281 (22.1)	301 (21.3)	346 (22.0)	375 (20.3)	265 (19.2)	247 (23.2)
41–42 years old	37 (19.1)	46 (17.8)	47 (15.5)	63 (18.1)	62 (14.9)	67 (12.7)	100 (16.0)	81 (13.1)	120 (16.0)	75 (13.8)	70 (15.7)
>42 years old	7 (6.5)	12 (7.2)	12 (5.7)	25 (9.6)	24 (6.4)	30 (6.7)	39 (7.5)	39 (6.9)	32 (4.1)	32 (6.1)	25 (6.7)

embryonic competence due to impaired aging, particularly regarding the increased incidence of aneuploidy and possibly decreased mitochondrial activity.²³ Our finding is also consistent with that of Bowolaksono et al., which shows that women aging is in line with the decrease in Anti-Müllerian Hormone (AMH) and mitochondrial DNA (mtDNA).²⁴ One study found that a woman's age was positively correlated with the incidence and severity of tubal occlusive disease. It was proposed that women older than 35 years old had increased likelihood of infertility due to tubal factors and the pregnancy rate decreases.²⁵ According to research conducted by Indarwati et al. at the Sekar Clinic, Dr. RSUD. Moewardi, Surakarta, women with reproductive organ abnormalities (ovulation disorders, tube and pelvic disorders, and uterine disorders) have 11.7 times higher infertility risk than without reproductive organ disorders.²⁶ Dewi et al. reported 15.8% of the women at the Tunjung Graha Clinic, Sanglah Hospital, had unexplained cause of infertility. It was discovered that 25.0% had problems with one of their fallopian tubes, while 75.0% had problems with both fallopian tubes. In this study, no women had uterine abnormalities, and 12.5% had endometriosis.²⁷

According to the latest WHO statistics, about 50–80 million people worldwide suffer from infertility, and male factors affect about 20%–30% of all cases of infertility. This is consistent with our findings, where male factors contribute to the majority of infertility cause. Dewi et al. reported that indications in childbearing couples at the IVF Clinic at Sanglah Hospital Denpasar were found to be more frequently due to male factors with spermatogenesis disorders in 46.0% patients, female factors due to fallopian tube factors in 38.1%, and both male and female factors in 11.1%. This can be caused by male factors with anatomical abnormalities such as hypospadias and micropenis, functional disorders such as severe erectile dysfunction, and spermatogenesis disorders such as oligo/terato/asthenozoospermia.^{27,28}

Another study showed the success of IVF program in couples of childbearing age who succeeded in getting pregnant was 23.8%, with 86.7% successfully giving birth and 13.3% had abortions, while 76.2% failed to get pregnant. The percentage of males and females of couples who managed to get pregnant at 20–35 years old were 29.0%, and 24.3%, respectively. This shows that couples of reproductive age were able to achieve pregnancy more often than non-reproductive age couples.²⁸

The present study demonstrates the condition of ART developments in Indonesia and its outcome. The identification of key areas that require improvements and a prospective registry on ART pregnancies can provide an opportunity to enhance access to infertility care.

AUTHOR CONTRIBUTIONS

All authors conceived the idea of the study and contributed to the study design. All authors performed the data collection, material preparation, processing of the data and interpretation of the IVF data in Indonesia. Budi Wiweko, Eliza Mansyur, Tita Yuningsih, Ivan Sini, Vita Silvana, Mila Maidarti, Achmad Kemal Harzif, Gita Pratama, Kanadi Sumapraja, Raden Muharam, Andon Hestiantoro, Soegiharto

Soebijanto, Nurin Aisiyah Listyasari, Batara Sirait, Hendy Hendarto, Tono Djuwantono, Binarwan Halim, Ilyas Angsar, Nusratuddin Abdullah, Putra Adnyana, Shofwal Widad, Samsulhadi Samsulhadi, Syarif Thaufik Hidayat, Hartanto Bayuaji, Wiryawan Permadi, Dedy Hendry and Syahnural Lubis had were actively involved in the data collection from the patients and data validation process from each IVF center. All authors contributed to manuscript revisions. All authors approved the final version of the manuscript and agree to be held accountable for the content therein.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data which support the findings of this research are available within the article.

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