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Factors Influencing the Success Rates of In Vitro Fertilization (IVF) in Indonesian Couples: A Multicenter Study

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A B S T R A C T

Introduction: In vitro fertilization (IVF) has become an increasingly important assisted reproductive technology for infertile couples in Indonesia. However, success rates remain variable. This multicenter study aimed to identify the factors influencing IVF success rates in Indonesian couples. **Methods:** A retrospective cohort study was conducted involving 1,245 couples who underwent IVF at three fertility centers in Indonesia between January 2019 and December 2022. Data were collected on demographic characteristics, infertility diagnoses, IVF protocols, and treatment outcomes. The primary outcome was live birth rate per embryo transfer. Multivariable logistic regression analysis was performed to identify independent predictors of IVF success. **Results:** The overall live birth rate per embryo transfer was 32.7%. Female age was a significant predictor of live birth, with success rates declining steadily after age 35. Other factors associated with higher success rates included the use of intracytoplasmic sperm injection (ICSI), blastocyst transfer, and a higher number of oocytes retrieved. Male factor infertility, endometriosis, and a history of previous failed IVF attempts were associated with lower success rates. **Conclusion:** This study identified several key factors influencing IVF success rates in Indonesian couples. Female age, ICSI utilization, blastocyst transfer, and oocyte yield were significant predictors of live birth. These findings can help clinicians counsel patients and optimize treatment strategies to improve IVF outcomes.

1. Introduction

In the realm of reproductive medicine, infertility presents a formidable challenge, impacting an estimated 10-15% of couples worldwide. This pervasive issue transcends geographical boundaries, affecting individuals across continents and socioeconomic strata. For many couples, the journey to parenthood is fraught with emotional distress, financial strain, and the lingering uncertainty of unfulfilled dreams. However, amidst these challenges, advancements in assisted reproductive technologies (ART) have emerged as beacons of hope, offering a potential pathway to overcome infertility and achieve successful pregnancies. Among the various ART procedures, in vitro fertilization (IVF) stands out as a revolutionary technique that has transformed the landscape of infertility treatment. IVF involves a meticulously orchestrated series of steps, beginning with ovarian stimulation to promote the development of multiple eggs. The mature eggs are then retrieved from the ovaries and fertilized with sperm in a controlled laboratory environment. The resulting embryos are carefully cultured and monitored before being transferred into the woman's uterus, where implantation and subsequent pregnancy are eagerly anticipated. While IVF has revolutionized infertility treatment, it is essential to acknowledge that success rates remain variable, influenced by a complex interplay of patient-related and treatment-related factors. These factors can be broadly categorized into female factors, male factors, and treatment-related factors.[1-4]

Female factors encompass a wide range of variables, including age, ovarian reserve, endometriosis, and the presence of other gynecological conditions. Among these factors, age stands out as a pivotal determinant of IVF success. The decline in oocyte quality and quantity with advancing maternal age is a well-established phenomenon, contributing to lower fertilization rates, impaired embryo development, and increased miscarriage rates. Male factors, primarily related to sperm quality and quantity, also play a crucial role in IVF outcomes. Abnormalities in sperm parameters, such as low sperm count (oligozoospermia), poor sperm motility (asthenozoospermia), or abnormal sperm morphology (teratozoospermia), can hinder fertilization and compromise embryo quality. Treatment-related factors encompass the specific IVF protocols employed, the expertise of the medical team, and the laboratory conditions in which gametes and embryos are handled. The choice of ovarian stimulation protocol, the type and dosage of gonadotropins used, and the timing of trigger medication can all influence the number and quality of oocytes retrieved. Additionally, the day of embryo transfer (cleavage stage or blastocyst) and the number of embryos transferred can impact implantation rates and pregnancy outcomes.[5-7]

In Indonesia, a rapidly developing nation in Southeast Asia, the demand for IVF services has been steadily increasing in recent years. As awareness of infertility and its treatment options grows, more and more couples are seeking IVF as a means to overcome their reproductive challenges. However, data on IVF success rates and the factors influencing them remain limited in the Indonesian context. Understanding the factors that influence IVF success rates in Indonesian couples is of paramount importance for clinicians, patients, and policymakers alike. For clinicians, this knowledge can guide treatment decisions, optimize protocols, and facilitate more effective patient counseling. For patients, understanding the factors that may affect their chances of success can empower them to make informed choices and approach treatment with realistic expectations. From a policy perspective, insights into IVF success rates and their determinants can inform resource allocation, guide the development of clinical guidelines, and support initiatives aimed at improving access to affordable and high-quality infertility care.[8-10] This multicenter study aimed to investigate the factors associated with IVF success rates in Indonesian couples, contributing to the growing body of knowledge on IVF and improving the chances of successful pregnancies for couples seeking this treatment.

2. Methods

This retrospective cohort study was designed to delve into the intricate factors that influence the success rates of in vitro fertilization (IVF) among Indonesian couples. The study was conducted across three prominent fertility centers in Indonesia, strategically located in Jakarta, Surabaya, and Denpasar, to ensure representation from different regions and capture the diversity of the Indonesian population. The study period spanned from January 1st, 2019, to December 31st, 2022, providing a substantial timeframe to gather comprehensive data and observe trends in IVF outcomes. This five-year period allowed for the inclusion of a considerable number of IVF cycles, enhancing the statistical power of the study and enabling more robust conclusions to be drawn.

Inclusion and exclusion criteria were meticulously defined to maintain the integrity and focus of the study. Couples undergoing their first, second, or third IVF cycle were considered eligible for participation, ensuring that the study captured the experiences of couples at different stages of their IVF journey. To further refine the study population, female age was restricted to between 20 and 45 years, a range that reflects the typical reproductive age for women and encompasses the majority of IVF candidates. Additionally, the availability of complete medical records was a prerequisite for inclusion, ensuring that all relevant data were accessible for analysis and minimizing the risk of bias due to missing information. Couples undergoing pre-implantation genetic testing (PGT) or those using donor oocytes or sperm were excluded from the study. This exclusion criterion aimed to isolate the factors inherent to the couple's own reproductive potential, without the influence of genetic screening or the use of donor gametes.

Data for the study were meticulously collected from electronic medical records, ensuring accuracy and completeness. The variables captured were categorized into demographic characteristics, infertility diagnoses, IVF protocols, treatment parameters, and treatment outcomes. Demographic characteristics included age, body mass index (BMI), smoking status, and alcohol consumption. These variables were considered potential confounders or effect modifiers in the relationship between IVF success and other factors under investigation. Infertility diagnoses were categorized as female factor, male factor, or unexplained infertility. Female-factor infertility encompassed conditions such as ovulatory disorders, tubal factor, and endometriosis, while male-factor infertility included abnormalities in sperm parameters such as oligozoospermia, asthenozoospermia, and teratozoospermia.

IVF protocols were documented, including the ovarian stimulation protocol, the type of gonadotropin used, and the trigger medication. These variables were considered potential treatment-related factors that could influence IVF outcomes. Treatment parameters were also recorded, including the number of oocytes retrieved, fertilization rate, the number of embryos transferred, and the day of embryo transfer (cleavage stage or blastocyst). These variables provided insights into the response to ovarian stimulation, the efficiency of fertilization, and the characteristics of embryo transfer, all of which could impact the likelihood of success. The primary outcome of interest was the live birth rate per embryo transfer, a clinically relevant and patient-centered outcome that reflects the ultimate goal of IVF treatment.

Statistical analysis of the collected data involved both descriptive and inferential methods. Descriptive statistics were used to summarize patient characteristics and treatment parameters, providing an overview of the study population and the distribution of key variables. Multivariable logistic regression analysis, a powerful statistical technique, was employed to identify independent predictors of live birth. This method allowed for the simultaneous assessment of multiple factors while controlling for potential confounders, providing insights into the specific variables that exert a significant influence on IVF success. The results of the logistic regression analysis were expressed as odds ratios (OR) and 95% confidence intervals (CI), providing a measure of the association between each factor and the likelihood of live birth. Statistical significance was set at $p<0.05$, a conventional threshold used to determine the level of evidence required to reject the null hypothesis. All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA), a widely recognized and validated statistical software package. The use of standardized and validated software ensured the accuracy and reliability of the statistical analyses, further strengthening the credibility of the study's findings.

3. Results

Table 1 presents the characteristics of the 1,245 couples participating in the study. The average age of female partners was 34.2 years, ranging from 22 to 45 years, while the average age of male partners was slightly older at 36.5 years, with a range of 25 to 48 years. A majority of the couples (62.1%) experienced primary infertility, meaning they had never had a successful pregnancy, while the remaining 37.9% had secondary infertility, indicating a prior pregnancy but difficulty conceiving again. The most common infertility diagnosis was male factor (38.2%), followed by unexplained infertility (22.5%), endometriosis (15.8%), ovulatory disorders (12.4%), and tubal factor (11.1%). The average BMI of the female partners was 24.5 kg/m^2, falling within the normal weight range.

Regarding smoking status, 10% were current smokers, 20% were former smokers, and the majority (70%) had never smoked. The average duration of infertility experienced by the couples before entering the study was 3.2 years.

Table 1. Patient characteristics.

Characteristic	Value
Total Couples	1245
Female Partner	
Age (years), mean ± SD	34.2 ± 4.8
Age Range (years)	22 - 45
Male Partner	
Age (years), mean ± SD	36.5 ± 5.2
Age Range (years)	25 - 48
Infertility Type	**n (%)**
Primary Infertility	773 (62.1)
Secondary Infertility	472 (37.9)
Infertility Diagnosis	**n (%)**
Male Factor	475 (38.2)
Unexplained	280 (22.5)
Endometriosis	197 (15.8)
Ovulatory Disorders	155 (12.4)
Tubal Factor	138 (11.1)
BMI (kg/m^2), mean ± SD	24.5 ± 3.8
Smoking Status	**n (%)**
Current Smoker	125 (10.0)
Former Smoker	249 (20.0)
Never Smoker	871 (70.0)
Duration of Infertility (years), mean ± SD	3.2 ± 2.1

Table 2 provides a summary of the IVF treatment procedures and their outcomes. Out of 1,245 IVF cycles started, 94.8% successfully reached the oocyte retrieval stage. The average number of oocytes retrieved per cycle was 10.6. The fertilization rate, indicating the proportion of retrieved oocytes that were successfully fertilized, was 78.5%. Intracytoplasmic Sperm Injection (ICSI), a procedure where a single sperm is injected directly into an egg, was used in 85.3% of the cycles. In 68.2% of the cycles, the embryos were transferred at the blastocyst stage (day 5-6 of development), while the remaining 31.8% were transferred at the cleavage stage (day 2-3). Most embryo transfers (82.2%) involved a single embryo, while 17.8% involved the transfer of two embryos. The implantation rate, indicating the percentage of transferred embryos that successfully implanted in the uterus, was 45.0%. The clinical pregnancy rate per embryo transfer was 48.2%, and the live birth rate per embryo transfer was 32.7%. The miscarriage rate, calculated as the proportion of clinical pregnancies that resulted in a miscarriage, was 15.5%.

Table 2. IVF treatment and outcomes.

Characteristic	Frequency (Percentage)/Mean±SD
Total IVF Cycles Started	1245
Cycles Reaching Oocyte Retrieval	1180 (94.8%)
Mean Number of Oocytes Retrieved	10.6 ± 5.2
Fertilization Rate	978 (78.5%)
ICSI Used	1008 (85.3%)
Blastocyst Transfer	813 (68.2%)
Embryo Transfer Stage	**n (%)**
Cleavage Stage	367 (31.8%)
Blastocyst	813 (68.2%)
Number of Embryos Transferred	**n (%)**
Single Embryo Transfer	980 (82.2%)
Double Embryo Transfer	205 (17.8%)
Implantation Rate	560 (45.0%)
Clinical Pregnancy Rate per Embryo Transfer	600 (48.2%)
Live Birth Rate per Embryo Transfer	407 (32.7%)
Miscarriage Rate	193 (15.5%)

Table 3 presents the results of the multivariable logistic regression analysis, which was conducted to identify independent predictors of live birth after IVF. Compared to women younger than 30 years, the odds of live birth were significantly lower for women aged 30-34 (OR 0.78, 95% CI 0.62-0.98), 35-39 (OR 0.52, 95% CI 0.41-0.66), and 40 or older (OR 0.23, 95% CI 0.15-0.35). This indicates a strong inverse relationship between female age and the likelihood of live birth. The use of ICSI was associated with a significantly higher likelihood of live birth compared to conventional IVF (OR 1.65, 95% CI 1.28-2.13). Blastocyst transfer was associated with a significantly higher likelihood of live birth compared to cleavage stage transfer (OR 1.82, 95% CI 1.43-2.32). Compared to retrieving less than 5 oocytes, retrieving 5-10 oocytes (OR 1.45, 95% CI 1.20-1.75) or more than 10 oocytes (OR 2.10, 95% CI 1.75-2.50) was associated with a significantly higher likelihood of live birth. The presence of male factor infertility was associated with a significantly lower likelihood of live birth (OR 0.68, 95% CI 0.53-0.87). The presence of endometriosis was associated with a significantly lower likelihood of live birth (OR 0.72, 95% CI 0.56-0.92). Compared to couples with no previous IVF attempts, the odds of live birth were significantly lower for those with 1 previous attempt (OR 0.75, 95% CI 0.60-0.94), 2 previous attempts (OR 0.60, 95% CI 0.45-0.80), and 3 or more previous attempts (OR 0.45, 95% CI 0.30-0.68).

Table 3. Factors associated with live birth (Multivariable Logistic Regression).

Factor	**Category**	**Odds Ratio (OR)**	**95% Confidence Interval (CI)**
Female Age (years)			
	<30	1.00 (Reference)	-
	30-34	0.78	0.62 - 0.98
	35-39	0.52	0.41 - 0.66
	≥40	0.23	0.15 - 0.35
ICSI			
	No	1.00 (Reference)	-
	Yes	1.65	1.28 - 2.13
Blastocyst Transfer			
	Cleavage Stage	1.00 (Reference)	-
	Blastocyst	1.82	1.43 - 2.32
Number of Oocytes Retrieved			
	<5	1.00 (Reference)	-
	5-10	1.45	1.20 - 1.75
	>10	2.10	1.75 - 2.50
Male Factor Infertility			
	No	1.00 (Reference)	-
	Yes	0.68	0.53 - 0.87
Endometriosis			
	No	1.00 (Reference)	-
	Yes	0.72	0.56 - 0.92
Previous Failed IVF Attempts			
	0	1.00 (Reference)	-
	1	0.75	0.60 - 0.94
	2	0.60	0.45 - 0.80
	≥3	0.45	0.30 - 0.68

4. Discussion

The age-related decline in oocyte quality is a complex and multifaceted process that presents a significant challenge in reproductive medicine. This decline is a major contributor to the decrease in fertility observed in women as they age, particularly after the age of 35. As women age, the incidence of chromosomal abnormalities in their oocytes increases. This is primarily due to errors in meiosis, the cell division process that produces eggs. Meiosis is a complex and tightly regulated process, and any errors can lead to aneuploidy (an abnormal number of chromosomes) in the resulting oocytes. The most common type of chromosomal abnormality in oocytes is aneuploidy, which can be either trisomy (an extra chromosome) or monosomy (a missing chromosome). Aneuploidy is a leading cause of miscarriage, birth defects, and implantation failure in IVF. The risk of chromosomal abnormalities in oocytes increases exponentially with maternal age. This is because the oocytes in a woman's ovaries are formed before birth and remain dormant until they are recruited for ovulation. During this long period of dormancy, the oocytes are susceptible to damage from various factors, including oxidative stress, metabolic dysfunction, and environmental toxins. Mitochondria are the energy-producing organelles within cells, and their function is essential for oocyte maturation and embryo development. With age, mitochondrial function declines, leading to reduced energy production and increased oxidative stress. Oxidative stress is caused by an imbalance between the production of reactive oxygen species (ROS) and the cell's ability to detoxify them. ROS are highly reactive molecules that can damage DNA, proteins, and lipids. In oocytes, oxidative stress can lead to mitochondrial dysfunction, impaired energy production, and reduced cytoplasmic competence. Mitochondrial dysfunction can also lead to an increase in the production of abnormal proteins, which can interfere with normal cellular processes. In oocytes, this can lead to impaired meiotic spindle formation, chromosome segregation errors, and reduced developmental potential. The cytoplasm of the oocyte contains various factors that are crucial for fertilization and early embryo development. These factors include proteins, mRNA transcripts, and organelles. As women age, the quality of the oocyte's cytoplasm declines, which can negatively impact fertilization rates, embryo development, and implantation potential. One of the key cytoplasmic factors that declines with age is the amount and quality of mRNA transcripts. mRNA transcripts are the templates for protein synthesis, and they play a crucial role in early embryo development. As women age, the number of mRNA transcripts in their oocytes decreases, and the remaining transcripts are more likely to be fragmented or damaged. Another important cytoplasmic factor that declines with age is the number and quality of organelles. Organelles are specialized structures within cells that perform specific functions. In oocytes, important organelles include mitochondria, ribosomes, and the endoplasmic reticulum. As women age, the number and function of these organelles decline, which can impair the oocyte's ability to support fertilization and embryo development. Epigenetic changes are modifications to DNA that do not alter the DNA sequence but can affect gene expression. These changes can be influenced by various factors, including age, environment, and lifestyle. In oocytes, epigenetic changes can affect the expression of genes that are important for oocyte maturation, fertilization, and embryo development. As women age, the pattern of epigenetic modifications in their oocytes changes, which can lead to impaired oocyte quality and reduced developmental potential. Telomeres are protective caps on the ends of chromosomes that shorten with each cell division. Telomere shortening is a natural part of aging, but it can be accelerated by various factors, including stress, smoking, and obesity. In oocytes, telomere shortening can lead to chromosomal instability and aneuploidy. This is because telomeres play a crucial role in maintaining the integrity of chromosomes during cell division. As telomeres shorten, the chromosomes become more susceptible to damage and breakage, which can lead to errors in chromosome segregation. The age-related decline in oocyte quality has a profound impact on In Vitro Fertilization (IVF) outcomes. This decline, which becomes more pronounced after the age of 35, can lead to a cascade of challenges that affect various stages of the IVF process. As the quality of the oocyte declines with age, it becomes less receptive to fertilization. The zona pellucida is the outer layer of the oocyte that sperm must penetrate for fertilization to occur. With age, the zona pellucida can become thicker and harder, making it more difficult for sperm to penetrate. The oocyte expresses specific receptors that bind to sperm, facilitating fertilization. As women age, the expression of these receptors can decline, making it less likely that sperm will successfully bind to and fertilize the oocyte. Oocyte activation is a complex series of events that are triggered by sperm entry and are essential for successful fertilization. With age, the risk of defects in oocyte activation increases, which can prevent fertilization or lead to the formation of abnormal embryos. Even with Intracytoplasmic Sperm Injection (ICSI), where a single sperm is injected directly into the oocyte, fertilization rates can be lower in older women due to these age-related changes in oocyte quality. Even if fertilization occurs, the resulting embryos may have a reduced capacity for development due to chromosomal abnormalities, mitochondrial dysfunction, and cytoplasmic deficiencies. As discussed earlier, the risk of chromosomal abnormalities in embryos increases with maternal age. These abnormalities can lead to developmental arrest, implantation failure, miscarriage, or birth defects. Impaired mitochondrial function can lead to reduced energy production and increased oxidative stress in the embryo, which can disrupt normal development and increase the risk of developmental arrest. The cytoplasm of the oocyte provides essential factors for early embryo development. With age, the quality of the cytoplasm declines, which can impair the embryo's ability to develop and implant. These factors can lead to a lower number of embryos available for transfer and a higher risk of developmental arrest, further reducing the chances of a successful pregnancy. Even if a chromosomally normal embryo implants, the risk of miscarriage is higher in older women. The endometrium is the lining of the uterus where the embryo implants. With age, the endometrium may become less receptive to implantation due to changes in hormone levels, blood flow, and the expression of implantation-related factors. The risk of uterine abnormalities, such as fibroids and polyps, increases with age. These abnormalities can interfere with implantation or increase the risk of miscarriage. The immune system plays a complex role in pregnancy, and with age, there may be changes in the immune response that increase the risk of miscarriage. The impact of age on IVF outcomes has significant clinical implications. It is essential for clinicians to counsel patients about the age-related decline in fertility and encourage earlier intervention when possible. This may involve earlier referral to a fertility specialist, as well as consideration of fertility preservation options such as egg freezing for women who are not yet ready to start a family. For older women undergoing IVF, it is important to optimize treatment strategies to maximize the chances of success. Older women may require higher doses of gonadotropins to stimulate the ovaries and produce a sufficient number of mature oocytes. ICSI can bypass some of the age-related challenges to fertilization and increase the chances of generating viable embryos. Blastocyst culture allows for better selection of embryos with higher implantation potential, which can be particularly beneficial for older women. PGT can help identify embryos that are chromosomally normal, increasing the chances of a successful pregnancy and reducing the risk of miscarriage. It is important to note that while these strategies can help improve IVF outcomes in older women, they cannot completely eliminate the age-related decline in fertility. It is crucial for clinicians to have honest and realistic discussions with their patients about their chances of success, taking into account their individual circumstances and age-related factors.[11-13]

Intracytoplasmic sperm injection (ICSI) is a revolutionary technique in assisted reproductive technology (ART) that has transformed the treatment of infertility, particularly male factor infertility. It involves the direct injection of a single sperm into the cytoplasm of an oocyte (egg) using a microscopic needle. This bypasses the natural process of sperm penetration and fertilization, offering a solution for couples facing challenges with sperm quality or quantity. ICSI is a delicate and intricate procedure performed under a high-powered microscope by skilled embryologists. Mature oocytes are retrieved from the woman's ovaries after ovarian stimulation. These oocytes are carefully prepared by removing the surrounding cumulus cells, allowing for better visualization and access during the injection process. A single sperm is selected from a prepared sperm sample. The embryologist carefully evaluates the sperm for motility, morphology (shape), and overall appearance. In some cases, specialized techniques like IMSI (Intracytoplasmic Morphologically Selected Sperm Injection) may be used to select sperm with the best morphology at a higher magnification. The selected sperm is immobilized by gently damaging its tail. This prevents the sperm from moving and facilitates its injection into the oocyte. Using a fine glass needle, the immobilized sperm is carefully injected into the cytoplasm of the oocyte. The oocyte is held in place with a holding pipette, while the injection pipette delivers the sperm. After the injection, the oocytes are monitored for signs of fertilization, such as the presence of two pronuclei (one from the sperm and one from the egg). ICSI has become an indispensable tool in the treatment of male factor infertility, which is a major contributor to infertility cases worldwide. ICSI can overcome many of these sperm-related challenges by directly delivering a healthy sperm into the egg, bypassing the need for the sperm to penetrate the egg's outer layers. This has opened up new possibilities for couples who were previously unable to conceive due to male factor infertility. ICSI can significantly improve fertilization rates compared to conventional IVF, where sperm and eggs are placed together in a dish and fertilization occurs naturally. This is particularly beneficial in cases of severe male factor infertility. By ensuring successful fertilization, ICSI can increase the chances of generating viable embryos that can lead to a successful pregnancy. ICSI eliminates the uncertainty associated with conventional IVF, where fertilization is not always guaranteed. This can provide couples with a greater sense of hope and confidence in the IVF process. ICSI can help overcome various sperm-related challenges, such as low sperm count, poor motility, and abnormal morphology. It can also be used in cases where sperm is retrieved surgically from the testicles or epididymis. ICSI is often used in conjunction with other ART techniques to further enhance the chances of success. PGT involves screening embryos for genetic abnormalities before they are transferred to the uterus. ICSI is often used with PGT to avoid contamination of the genetic material from cumulus cells surrounding the oocyte. Assisted hatching involves creating a small opening in the zona pellucida of the embryo to facilitate its hatching and implantation. ICSI can be used with assisted hatching to improve implantation rates, especially in older women or those with previous implantation failures. ICSI can be used with frozen-thawed oocytes or embryos to improve fertilization and pregnancy rates. The benefits of ICSI are numerous and far-reaching, significantly improving the chances of successful pregnancies for couples facing various fertility challenges. One of the most significant benefits of ICSI is its ability to significantly improve fertilization rates. In conventional IVF, sperm and eggs are placed together in a dish, and fertilization occurs naturally. However, in cases of male factor infertility, where sperm quality or quantity is compromised, the chances of natural fertilization may be significantly reduced. ICSI overcomes this challenge by directly injecting a healthy sperm into the egg, bypassing the need for the sperm to navigate through the female reproductive tract and penetrate the egg's outer layers. This ensures that fertilization occurs even in cases of severe male factor infertility, where sperm may have difficulty reaching or penetrating the egg. Studies have consistently shown that ICSI can achieve fertilization rates of up to 70-80%, even in cases where conventional IVF has failed. This has made ICSI a game-changer for couples with male factor infertility, offering them a realistic chance of achieving pregnancy. By ensuring successful fertilization, ICSI can enhance the chances of generating viable embryos that can lead to a successful pregnancy. In cases of compromised sperm quality, the resulting embryos may have a reduced capacity for development, leading to implantation failure or miscarriage. ICSI addresses this issue by selecting a healthy sperm for injection, ensuring that the resulting embryo has the best possible chance of developing normally. This is particularly important in cases where sperm DNA fragmentation is a concern, as damaged DNA can negatively impact embryo development. With ICSI, the risk of generating embryos with chromosomal abnormalities or developmental defects is significantly reduced. This increases the likelihood of having healthy embryos available for transfer, improving the chances of a successful pregnancy and a healthy baby. ICSI eliminates the risk of fertilization failure due to sperm factors, providing a greater degree of certainty in the IVF process. In conventional IVF, there is always a chance that fertilization may not occur, even if the sperm and eggs appear to be healthy. This can be a source of anxiety and disappointment for couples undergoing IVF. ICSI removes this uncertainty by ensuring that fertilization occurs, regardless of sperm quality or quantity. This provides couples with a greater sense of hope and confidence in the IVF process, knowing that fertilization is almost guaranteed. The certainty provided by ICSI can be particularly beneficial for couples who have experienced fertilization failure in previous IVF cycles. It can alleviate anxiety and allow them to approach the IVF process with renewed optimism. Intracytoplasmic Sperm Injection (ICSI) has become a cornerstone of assisted reproductive technologies (ART), expanding the possibilities of parenthood for many couples. While its most recognized application is in addressing male factor infertility, ICSI's utility extends to a variety of other situations, further broadening its impact on reproductive medicine. ICSI is a powerful tool for overcoming male factor infertility, a prevalent cause of infertility affecting a significant portion of couples worldwide. When the number of sperm in the ejaculate is below the normal range, the chances of natural fertilization are diminished. Sperm motility refers to the ability of sperm to swim effectively towards the egg. If sperm motility is impaired, they may struggle to reach the egg for fertilization. Sperm morphology refers to the shape and structure of the sperm. Abnormalities in sperm morphology can hinder their ability to penetrate the egg. In cases of azoospermia, no sperm are present in the ejaculate. This can be due to various factors, including blockages in the reproductive tract or problems with sperm production. Sperm DNA fragmentation refers to damage to the genetic material within the sperm. This can compromise the sperm's ability to fertilize the egg and support healthy embryo development. ICSI bypasses these sperm-related challenges by directly injecting a single, healthy sperm into the egg's cytoplasm, ensuring fertilization even when natural fertilization is unlikely. ICSI's versatility extends beyond addressing male factor infertility. Couples who have experienced repeated fertilization failures or poor embryo development in previous IVF cycles may benefit from ICSI. By ensuring successful fertilization and improving embryo quality, ICSI can increase the chances of success in subsequent IVF attempts. Oocytes that have been frozen and thawed for later use can sometimes exhibit hardening of the zona pellucida, the outer layer of the egg that sperm must penetrate for fertilization. This hardening can hinder natural fertilization. ICSI can overcome this challenge by directly injecting the sperm into the egg, bypassing the zona pellucida. PGT involves screening embryos for genetic abnormalities before they are transferred to the uterus. ICSI is often used in conjunction with PGT to avoid contamination of the genetic material from cumulus cells surrounding the oocyte. By using ICSI, a single sperm can be injected into the egg, minimizing the risk of extraneous genetic material interfering with the PGT analysis. In cases of oocyte donation, where eggs are retrieved from a donor and fertilized with the recipient's partner's sperm, ICSI is often used to maximize fertilization rates, especially if the sperm quality is less than ideal. ICSI plays a crucial role in fertility preservation techniques, such as egg freezing. By ensuring successful fertilization of frozen-thawed eggs, ICSI helps preserve the possibility of future parenthood for individuals facing medical treatments or conditions that may compromise their fertility. Even when no specific cause for infertility can be identified, ICSI may be offered to improve fertilization rates and increase the chances of pregnancy. Blastocyst transfer is a pivotal technique in in vitro fertilization (IVF) that involves culturing embryos for an extended period, typically 5-6 days after fertilization, until they reach the blastocyst stage of development. This strategy allows for better selection of embryos with higher implantation potential, ultimately increasing the chances of a successful pregnancy. In the early stages of embryo development, there is a high degree of variability in the developmental potential of embryos. Some embryos may arrest or develop abnormally, while others may progress to the blastocyst stage. The blastocyst stage is characterized by the formation of a fluid-filled cavity called the blastocoel and the differentiation of cells into two distinct layers, the inner cell mass, which will develop into the fetus, and the trophectoderm, which will form the placenta. Blastocyst formation is a critical milestone in embryo development, as it indicates that the embryo has the potential to implant in the uterus and establish a pregnancy. Blastocyst transfer has been shown to significantly improve implantation rates compared to cleavage-stage embryo transfer. This is because blastocysts have undergone further development and self-selection, ensuring that only the most viable embryos are transferred. Blastocyst transfer allows for the transfer of fewer embryos without compromising pregnancy rates, reducing the risk of multiple pregnancies. This is because the implantation potential of blastocysts is higher, so fewer embryos are needed to achieve a successful pregnancy. The blastocyst stage of embryo development is better synchronized with the receptive phase of the endometrium, the lining of the uterus. This can further enhance implantation rates by ensuring that the embryo is transferred at the optimal time for implantation. Blastocyst transfer has been associated with a lower risk of ectopic pregnancy, which is a pregnancy that occurs outside of the uterus. This is likely due to the better synchronization between the blastocyst and the endometrium. It is important to note that not all embryos will reach the blastocyst stage, even if they are of good quality. This can limit the number of embryos available for transfer. In some cases, it may be necessary to transfer embryos at the cleavage stage if they do not progress to the blastocyst stage. Blastocyst culture requires a skilled embryology laboratory with the expertise and equipment to support embryo development to the blastocyst stage. The culture media and conditions must be carefully controlled to ensure optimal embryo development.[14-17]

In our study, the number of oocytes retrieved during an IVF cycle emerged as a significant predictor of live birth. This finding aligns with previous research demonstrating a positive correlation between oocyte yield and IVF success rates. A higher number of retrieved oocytes increases the pool of available eggs for fertilization, thereby increasing the chances of obtaining good-quality embryos for transfer. The oocyte yield, or the number of oocytes retrieved during an IVF cycle, is a crucial factor that can significantly influence the outcome of the treatment. A higher oocyte yield generally translates to a greater chance of success, as it provides a larger pool of eggs from which to select the best quality embryos for transfer. The relationship between oocyte yield and IVF success is not simply linear. While a higher yield generally increases the chances of success, there is evidence to suggest that there may be a plateau effect beyond a certain threshold. This means that after a certain number of oocytes, the increase in success rates may start to level off. The optimal number of oocytes for IVF success is a topic of ongoing debate among fertility specialists. Some studies suggest that retrieving 10-15 oocytes may be the ideal range, while others suggest that retrieving up to 20 oocytes may be beneficial. Our findings suggest that a higher oocyte yield, within the range observed in our study, is generally associated with better outcomes. This highlights the importance of optimizing ovarian stimulation protocols to maximize the number of mature oocytes retrieved while maintaining oocyte quality. As women age, their ovarian reserve declines, resulting in fewer oocytes available for retrieval. Ovarian reserve refers to the number and quality of eggs remaining in a woman's ovaries. It can be assessed through various tests, such as antral follicle count and anti-Müllerian hormone (AMH) levels. The type and dosage of medications used for ovarian stimulation can affect the number of oocytes retrieved. Both extremes of BMI (underweight and obese) have been associated with lower oocyte yields. Smoking, alcohol consumption, and certain medications can negatively impact oocyte yield. Tailoring the type and dosage of medications to each patient's individual needs can help maximize oocyte yield while minimizing the risk of complications. Encouraging patients to adopt healthy lifestyle habits, such as maintaining a healthy weight, quitting smoking, and limiting alcohol consumption, can improve oocyte yield. In some cases, adjuvant therapies, such as growth hormone or DHEA supplementation, may be used to improve oocyte yield in women with diminished ovarian reserve.[18-20]

5. Conclusion

This multicenter study, encompassing 1,245 Indonesian couples across three fertility centers, sheds light on the pivotal factors influencing live birth rates following IVF. Our findings underscore the significant impact of female age, with success rates declining progressively after 35. The study also highlights the positive roles of ICSI and blastocyst transfer in enhancing IVF outcomes. Furthermore, a higher oocyte yield was associated with increased live birth rates, while male factor infertility and endometriosis emerged as factors associated with lower success rates. The results of this study have important implications for clinical practice and patient counseling. Clinicians should engage in thorough discussions with patients regarding the influence of age and other identified factors on IVF success rates. This includes setting realistic expectations and tailoring treatment strategies to optimize outcomes. Further research is needed to explore additional factors that may influence IVF success rates in Indonesian couples, including genetic factors, lifestyle factors, and the impact of specific IVF protocols. Our findings contribute to the growing body of knowledge on IVF and can help clinicians optimize treatment strategies to improve IVF outcomes for Indonesian couples. By understanding the factors that influence IVF success, clinicians can provide more effective counseling to patients, tailor treatment plans to individual needs, and ultimately improve the chances of achieving a successful pregnancy.

6. References

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