



MAGNITUDE OF IN VITRO FERTILIZATION SUCCESS AMONG COUPLES
TREATED IN CENTER FOR FERTILITY AND REPRODUCTIVE MEDICINE,
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List of Abbreviations

ART	Assisted Reproductive Technology
AMH	Anti Mullerian Hormone
CFRM	Center for Fertility and Reproductive Medicine
FSH	Follicle Stimulating Hormone
IVF	In-Vitro Fertilization
ICSI	Intra Cytoplasmic Sperm Injection
ETB	Ethiopian Birr
LH	Luteinizing Hormone
IUI	Intrauterine Insemination
SPSS	Statistical Package of Social Science
SPHMMC	St. Paul Hospital Millennium Medical College
TSH	Thyroid Stimulating Hormone
WHO	World Health Organization

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Abstract

Introduction: Infertility is a failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse. In vitro fertilization is an important assisted reproductive technology to have a child among infertile couples. It is very significant to improve the success rate following In vitro Fertilization by monitoring for its determining factors. However, there is lack of adequate data on magnitude and determinants of In vitro fertilization success in Ethiopia. Thus, this study determined the magnitude and associated factors of In vitro fertilization success in Center for Fertility and Reproductive Medicine, Ethiopia.

Methodology: Institution based retrospective record review was conducted in Center for Fertility and Reproductive Medicine, Addis Ababa, Ethiopia. Study included 924 couples who had In-vitro Fertilization from September 1, 22 to August 31, 23. Data were collected from February 1 to March 30, 2023 using pretested and structured questioner from couples electronic medical record. Data was collected electronically using KOBO tool, downloaded on excel format and exported to SPSS version 26 for analysis. Logistic regression used to assess predictors of success of In vitro fertilization. Odds ratio, P value < 0.05 with 95% CI considered as a significant variable. Tables, figures, and text were used to report the findings.

Result: This study found that the magnitude of In vitro fertilization success was 34.7% (95% CI (32.0-36.0). female partner age > 35 years (AOR 0.52, 95% CI 0.36-0.75, $p < 0.001$), duration of infertility <5 years (AOR 1.57, 95% CI 1.16-2.13, $p = 0.004$), number of retrieved oocytes ≤ 4 (AOR 0.70, 95% CI 0.50-0.99, $p = 0.04$), day 3 embryo transfer (AOR, 0.29 95% CI 0.20-0.41, $p < 0.001$), and antra follicular count < 5 (AOR 0.55, 95% CI 0.35-0.85, $p = 0.007$) were the predictors of success of In vitro fertilization.

Conclusion: The magnitude of In vitro fertilization success in the study area were found to be comparable to the level of expected success in the European Society of Human Reproduction and Embryology guideline which is 35-40%. This study suggested an individual-based treatment for couples with females age >35, and >5 duration of infertility, <4 retrieved oocytes, day 3 embryo transfer, and <5 antra follicular count to improve their chances of In vitro fertilization success.

Keywords: Assisted Reproductive Technology, In-Vitro Fertilization, Infertility, Center for Fertility and Reproductive Medicine, Ethiopia

1. Introduction

1.1. Background

Infertility is a disease characterized by the failure to achieve a clinical pregnancy after 12 months of regular and unprotected intercourse (1). Globally, it is estimated that 8 to 12% of reproductive age group couples are infertile (1,2). A 20 to 30% of infertility cases are caused due to male factors, 20-30% are result of female infertility and 25-40% are combined, and 10-20% cases is unknown(3).

Assisted Reproductive Technology (ART), is the mainstay of treatment for infertility. It includes; In-vitro Fertilization (IVF), Intra Cytoplasmic Sperm Injection (ICSI), Intrauterine Insemination (IUI), frozen embryo transfer, egg freezing, preimplantation genetic diagnosis for the disorder, and Laser Assisted Hatching. Of all ART type, IVF is the majorly used procedure (4–6). The first successful IVF treatment in humans was performed in 1978 in England (6). In Ethiopia, the first IVF treatment started at Alikima Fertility Center followed by the first public fertility center named Centre for Fertility and Reproductive Medicine (CFRM) St. Paul's Hospital Millennium Medical College in 2019, third New Leaf clinic and fourth is Ethio Life infertility clinic.

The term ‘in-vitro’ means outside the living organism, as eggs mature in vivo (inside) in the ovary and embryos develop into pregnancy in the uterus, but the eggs are fertilized in a petri dish in the laboratory (4). The procedure is sometimes done together with ICSI, which is a single spermatozoon is injected into a mature oocyte (7,8) among female age greater than 35 and in case of male factor infertility (9). An IVF procedure also performed for women with a tubal disease like tube blockage or impaired tubal function, unexplained infertility, those with complaints of three and more years of infertility and those age 30 and above, and women age 36 and above with a diagnosis of mild to moderate endometriosis. Male infertility with the cause of sperm abnormality, which includes impairment on count or motility. The procedure is performed by suppressing the natural cycle with medication, helping women’s ovaries to produce more eggs using medications. Matured eggs collected from the ovaries, the retrieved eggs are mixed with sperm outside, and transfer 1 or 2 fertilized eggs (embryos) into the women womb. After all the procedure, a women wait for 2 weeks and check for blood test called chemical pregnancy confirmation, if the Human Chronic Gonadotropin hormone level is above 25mmgl, again after

two weeks an ultrasound test called biological confirmation will be conducted and confirmed whether the pregnancy is viable or non viable (4,5,7).

Success rate of IVF at globe is 30 % (10) and in Ethiopia is 30.1% (11). The success of IVF vary in different regions and determined by different factors. Thus, this study aimed to assess the magnitude and associated factors of IVF among IVF treated couples in the Center for Fertility and Reproductive Medicine, St. Paul's Hospital Millennium Medical College, Ethiopia, 2023.

1.2. Statement of the Problem

Globally, infertility affects nearly 1 in every 6 couples (4). The prevalence is high in lower and middle-income countries with infection-related tubal impairment being the most common reason. Over 180 million couples in sub-Saharan Africa countries are expected to suffer from primary or secondary infertility (12). In developing countries like Kenya, infertility accounts 26.1%(13), whereas in Ethiopia it is 27.6% with 14.4% primary and 13.2% secondary infertility (14). The mainstay of treatment for infertility is IVF. Over the past 40 years, access to IVF increased (15). From 1978 to date, over 10 million children globally have been conceived through IVF (16). And, the global IVF pregnancy reported to be 30% (10). The global need for IVF is predicted to be 1,500 cycles per million (17). Whereas, in developed countries 12.6% of couples seek infertility treatment per year (2). Due to underdeveloped infrastructure, cultural, religious, and legal barriers (18), even though the infertility treatment need is high, the first public IVF center in Ethiopia was started lately in 2019 and success rate estimated to be 30.1% (11).

World Health Organization (WHO) declared infertility as a global public health challenge (12). The impact of infertility in both developing and developed countries is broad. The consequence is double in developing countries with poor socioeconomic status, difference in availability of infertility treatment, and sociocultural values related to reproduction and childlessness (12). Infertility is a major cause for emotional stress and poor quality of life (19,20). The consequence extends from the lowest stage, level one to highest, level six. level one is fear, guilt, self-blame, and psychological stress, level two; marital status depression, polygamy, helplessness, level 3; social violence and social isolation, level 4; severe economic deprivation, moderate/severe violence, and total loss of social status, level 5; develops to suicide and starvation/disease and level 6; loss of dignity in death. In developed countries, due to the different availability in infertility treatment,

early diagnosis and care, and socio-cultural value to childlessness, the level goes reverse from level six to level one (12). In Ethiopia, where the community norm and culture are tight, childlessness is huge issue and acknowledgment of treatment options and success is minimal (4,19). Couples with successful IVF results an improved life satisfaction, minimized stress, worry, and resulted for a happy and long life ending (20).

Numerous aspects of IVF treatments have changed over time and extensive research had been conducted to improve IVF outcomes by addressing its influencing factors. In order to minimize the psychological stress and other consequences after unsuccessful IVF, clients could examine the probability of success based on their characteristics (21). Studies contradictory reported the outcome of IVF determined by many factors. Mostly, a woman has a cycle of IVF, she has about a 1 in 3 probability of becoming pregnant and giving birth (4). Younger age female's age < 35 has higher chance of success than 35 and more years old, the success decrease with age. By age 44, the probability of success is nearly 1 in 10 (4,11,22). Moreover, studies also reported that the success rate of IVF determined on, cause of infertility, medical response, standard of treatment, quality and quantity of egg/embryo, sperm count, level of Anti Mullerian Hormone (AMH), Estrogen level, level of Follicle Stimulating Hormone (FSH), level of Luteinizing Hormone (LH) and lifestyle (5,11,22–26).

Despite its significance, success of IVF has a number of determining factors. However, to my knowledge, there is still inadequate data on the magnitude and predictors of IVF success in the study area. And even though, success of IVF association to level of TSH (27), type of infertility (21,28), medical illness, endometrial thickness (29), and duration of infertility (28) identified in other studies, to my knowledge, no prior studies has examined this variables in the study area. Thus, this study aimed to determine the magnitude and associated factors of success of IVF in CFRM, Addis Ababa, Ethiopia.

1.3. Significance of the Study

Infertility is more than an individual health problem. It is a social issue. Considering this, WHO listed infertility as a global public health problem. It is a fact that having a child is a big chapter of a couple's life and a huge issue in the community. On the other side, childlessness results in unhappy married lives, divorces, and high levels of psychiatric morbidity. Moreover, infertile couples face social stigmatization and are publicly isolated. Thus, IVF is the best infertility treatment option to resolve the health and social consequence of infertility and leads to a happy and healthy family. Unsuccessful IVF aggravates adverse psychological problems including depression and anxiety. Repeated IVF results in financial, physical and emotional toll. Determining IVF success rate and associated factors will aid health policymakers to improve infertility treatment and maintain sustainability, will support care providers to characterize couples and to provide individual based care, decision making, and empower clients to examine the probability of success based on their own characteristics, which will minimize the consequence of unsuccessful IVF. Moreover, the study will fill the information gap and be a baseline for future researchers. Overall, the result will lead for the tall of IVF success, particular in study site and in Ethiopia at large.

2. Literature Review

A range of difference seen on the success rate of IVF (10,11,21,30). This is an indication that, the characteristics of infertile couples, the procedure and demographic factors determine the success rate of IVF. A summary of known and identified gaps illustrated as below.

2.1. Magnitude of Success of IVF

The global IVF success rate resulted to be 30% (10). In developed countries like America, 1.7% of births in the United States, resulted from IVF (15). Similarly, a retrospective study conducted in United States reported that the pregnancy rate following unstimulated IVF was 19.2% followed by 15.2% live birth (31). Besides, a historical cohort study conducted in Teheran, Iran reported IVF success rate as 81.2% (21). In Sub-Saharan Africa, in south Africa, Nambia, IVF success rate was 33.1% (32). In the meantime, a cross sectional study in Ethiopia determined the success rate of IVF as 30% (11).

2.2. Associated factors of success of In vitro fertilization

2.1.1. Demographic factors

Previous studies have emphasized, ageing of the female determines the success of an IVF (11,22,25). Aging result in decreased in the quantity, quality of retrieved oocytes, and decreased ovarian follicle reserves (22). Advanced female age > 35 years shows influence on the fertilization rate and a slight influence on embryonic development up to the blastocyst stage but results in a dramatic influence on the blastocyst aneuploidy rate. A cross-sectional study in Ethiopia reported those females with age >35 had a 61% decreased success rate with AOR 0.39 (95% CI, 0.18-0.83) (11). A historical cohort study in Iran reported, successful IVF deliveries was significant among younger age (21). This is consistence with cohort study in Brazil age <35 with AOR 15, (95% CI 5.9-41.6, P <0.001) (30).

Address of couples might potential associate with their lifestyle and might have an effect on success of IVF. A systematic review acknowledged, the association of an environment with success of IVF (33).

2.1.2. Clinical factors

Researches also revealed that the success of IVF determined by the cause of infertility. This is evidenced by a prospective cohort study conducted on women who had IVF after endometrial treatment with the success rate of 77% (24). The success rate is high after treatment of Polycystic Ovarian Syndrome. Whereas, success of IVF was poor among those with tubal disease, male factor, and endometriosis (21). This is consistent with a study in United States (34). In line with this, unidentified cause of infertility also resulted in poor success of IVF (21). Moreover, success rate of IVF was high in male cause of infertility (34). This is in line with a retrospective study conducted in Iran with Male factor (chi-square: 18.25, $P=0.003$) relation to success of IVF (21).

Additionally, primary infertility, showed its association with IVF fertilization disorder. Those with primary infertility are 1.30 times high likely to face failed IVF (OR:1.30 95% CI:1.16-1.46) (28). A historical cohort study in Tehiran disproved the finding, primary type of infertility (chi-square: 5.02, $P=0.025$) confirmed its higher probability of successful delivery (21). However, type of infertility have not showed association in other similar studies (11,21).

A retrospective cohort study by Amini P et al, 2021 also showed the association of IVF success among gravid or women with previous history of pregnancy. Those women who had previous experience of pregnancy or gravida one or more women were more successful than their counterparts (21).

It is a research finding that parity or number of delivery of viable fetus has a crucial impact on the success of IVF. According to, a study by Shana Ginar da Silva et.al, 2019, a population based cohort study conducted in southern Brazil reported that, null parity has lower chance of IVF success compared to their counterpart with (OR: 18.6, 95% CI: 4.1-85.2) (30).

It is a scientific evidence that regular menstrual cycle is a true figure of the normal female physiology. Which likely show the hormonal balance and normal ovulation and which might have

true potential in predicting the success of IVF. However, having regular menstrual cycle failed to show association with IVF outcome (11). This is supported by the study in Brazil, menstrual 3 months cycle prior to pregnancy, failed to show significance to outcome of IVF (COR 1.5, 95% CI 0.5-3.4) (30).

Duration of infertility is another important variable that affects IVF outcome. Zhang et al. (2022) retrospective cohort study in China reported, there was a nonlinear association between IVF fertilization rate and duration of infertility up until the turning point (4.8 years) (AOR, 0.91; 95% CI, 0.72-1.15)(36). This is in line with a retrospective observational study, which compares duration of infertility with pregnancy rate and live birth. Study reported those with infertility duration 1–2 years has 34.3% pregnancy and 25.7% live birth, 3–4 years duration of infertility has 21.8 % pregnancy rate and 14.9% birth and women with >4 years duration of infertility has 9.1% pregnancy rate and 4.5% live birth (37).

Studies have attempted to explain effect of semen fluid on IVF outcome (33). Sperm deformity is a trustworthy predictor of success of IVF (38). Those male partners with oligoasthenozoospermia had failure of fertilization comparing with normal semen parameters (39). Higher sperm motility and sperm total number are associated with higher chance of success of IVF(40). However, no significant association showed in some studies(11).

Cause of infertility, male factor showed a high likelihood of IVF success than female and unidentified causes. A study reported a significant association of male factors with success of infertility (chi-square: 18.25, df: 5, P=0.003) (21). However, this finding is not supported by other studies in the topic.

Beside to this, it is identified that, male partner with previous history of pregnancy has positive outcome of IVF comparing to their counterparts (40).

A retrospective study by Juan J. Tarin et. al (41) reported the association of female medical illness with success of IVF outcome. In comparison to healthy women, partners of sick women had lower odds of having live births (OR (95% CI) 0.704 (0.576-0.860)). Additional screening analyses showed that subclinical iodine deficiency hypothyroidism and autoimmune thyroiditis significantly reduced the chance of a live birth (OR (95% CI) 0.720 (0.608-0.853)).

A historical cohort study in Iran conducted on 4930 cycles examined the association of previous miscarriage with the success of current IVF outcome. This retrospective research identified, those females who had previous history of miscarriage (chi-square: 19.62, df: 2, $P < 0.001$) (21).

2.1.3. Procedure Related Factors

The stimulation protocol have also shown its effect on the success of IVF. An article exemplified the use of mild stimulation protocol is related with decreased in live birth from IVF (42). However, this is contradicted with another article which states, the pregnancy or live birth rates with mild-stimulation are comparable to those with conventional IVF. Moreover, the cumulative pregnancy outcome has been demonstrated to be same, despite having less numbers of oocytes or embryos available with milder ovarian stimulation (43). Likewise, lower doses of gonadotropins related with successful outcome (24).

Much of the current literature on IVF success pays particular attention to the number of oocytes retrieved, higher the number more success. This is evidenced on the study conducted in Iran (21), Ethiopia (11), and a retrospective study in china, number of oocyte retrieved < 5 was associated with low fertilization rate and fertilization failure (28).

Previous studies reveal that number of transferred embryo determine IVF success. A review article in Canada reported, elective single embryo transfer resulted a decreased pregnancy and birth to 33.1% (44), finding is similar to study in Iran (21). Unlikely, no association seen on a study in Ethiopia (11).

Experimental study in China associates, day of transferred embryo, blastocyst-stage, improved success of IVF (45). Likewise, a study reported cleavage stage does not improve IVF pregnancy and/or outcomes (46). However, a study by (Thomas et.al, 2021) failed to show statistical significance on day 5 embryo transfer (11).

Researches reviled the association of grade of embryo transfer with success of IVF. A retrospective study by Janati S et. al, 2022 reviled the higher likelihood of IVF success among Grade A or Grade 1 embryo transfer than there counterparts (47). This finding is consistent with a retrospective study by Bori L et.al, 2022. The study reported, there was a correlation between embryo score and the likelihood of implantation is 1.29 times higher OR=1.29; 95% CI (1.19-

1.39); P 0.001 for implantation and live birth is OR = 1.26; 95% CI (1.16-1.36); P 0.001 for live delivery) (48).

Outcome of previous IVF identified as major contributing factors for the success of IVF. A prospective study revealed that, the success of current IVF determined by the outcome of previous IVF. This is in line with a retrospective study in China (28).

It has been demonstrated that ICSI insemination method has shown success on IVF live birth. Male factor infertility without ICSI result in poor success of IVF. Previous research has indicated that “ICSI does not improve the reproductive outcomes of advanced-age patients undergoing conventional insemination for non-male factor infertility”(9).

Besides, Tien et.al, (2022) reported, Antra Follicular Count < 5 have no association with fertilization disorder and failed pregnancy (28). However, study by Thomas et al, reported, antra follicular count > 5 is related with good ovarian response (11).

2.1.4. Endometrial Thickness and Hormonal Level

A systematic review conducted on a review of 22 articles reported that the endometrial thickness has a relation with the success of IVF. Thin endometrium < 7mm related with less success of an IVF. Whereas thick endometrium >14mm had no effect on the success of IVF compared to medium thickness 7-14mm (29). This is contradicted with a retrospective study, endometrial thickness has no effect on the success of IVF (23).

Thomas et.al (11) examined the success of IVF in relation to day three FSH, reported the relation of . Moreover, Xin Liu (2022) conducted a retrospective cohort study revealed that the level of AMH related with early miscarriage following IVF/ICSI among age group <35. Similarly, “Young women with high serum AMH levels had a significantly higher risk of early miscarriage”. However, hormonal level doesn’t show miscarriage difference among age group >35 (49). This is in line with a study conducted by (Peuranpaa et. al, 2020) which reported that, “A low or moderately serum AMH level does not associate with miscarriage, non-visualized pregnancy loss or overall early pregnancy loss rate in the IVF/ICSI treatment”(50). Another retrospective comparative study also associated the inverse relation of Thyroid Stimulating Hormone (TSH) with IVF outcome. Women with high-normal quartile (2.5–4.5 mIU/L) TSH has 15% less live births after IVF compared to lower TSH quartiles (0.3–2.5 mIU/L) (27). In addition, increased

abnormal levels of Estradiol, have been identified as major contributing factors for the decreased response to ovulation inducing drugs resulting in reduced IVF success (33). Furthermore, even if day 3 Luteinizing Hormone (LH) has scientific impact on the reproductive system, it is failed to show statistical significance on success of IVF (11). Radin Dabbagh Rezaeiye et.al (33) assessed increased day 3 estradiol hormone linked to decreased response to ovulation-inducing drugs resulting in reduced IVF success prolactin hormone.

2.1.5. Ethical Aspect of IVF

Kjell Asplund (2020) reviewed IVF and the ethical issues in developed countries. In relation to age limits, in UK, women up to the age of 40 are limited to three IVF cycles and women up to the age of 42 limited to one cycle of IVF. IVF in single women and same-sex couples caused ethical arguments in relation to equity, non-discrimination, reproductive right, and children's safety. The legal restriction differ in different countries. 'Ownership' of gametes and embryos, preimplantary genetic testing, and egg freezing are other additional argumentative issues. This article also emphasized the impact of religion on IVF (51). IVF also employed as a component of government policy to boost birth rates. South Korea have been used as examples of such pronatalist nations (52). A systematic review by Anja von schondorf-Gleicher et.al emphasized beneficence, non-maleficence, respect for patient autonomy and justice, as the four key medical ethics principles of physicians and IVF centers (53). To the other side, IVF involves hazards for both the mother (ovarian stimulation, oocyte retrieval, and subsequent pregnancy) and the fetus, which vary depending on the mother's age and the number of fetuses (15). IVF patients are a vulnerable groups it is necessary to develop practice guidelines and an ethical framework to govern the practice of human assisted conception in Ethiopia, however, to the best of my knowledge, there has been no prior published research on ethical aspect of IVF in Ethiopia.

Large volume of studies in different countries retrospectively determined the success of IVF (18,21,30,48,50). Thomas et.al (2019) conducted a cross sectional study among 199 couples in the study area (11). Examined outcome variable association with demographic variables, female hormonal level, procedural factor, and sperm quality and quantity. However, the study conducted on small sample size (199) which underestimate statistical power and major variables were not included. Thus, this study is conducted with adequate sample, which improves the power and it

assessed additional variables. Below conceptual framework summarized variables included, their relation, and distance to the outcome variable (**Figure 1**).

Conceptual Framework

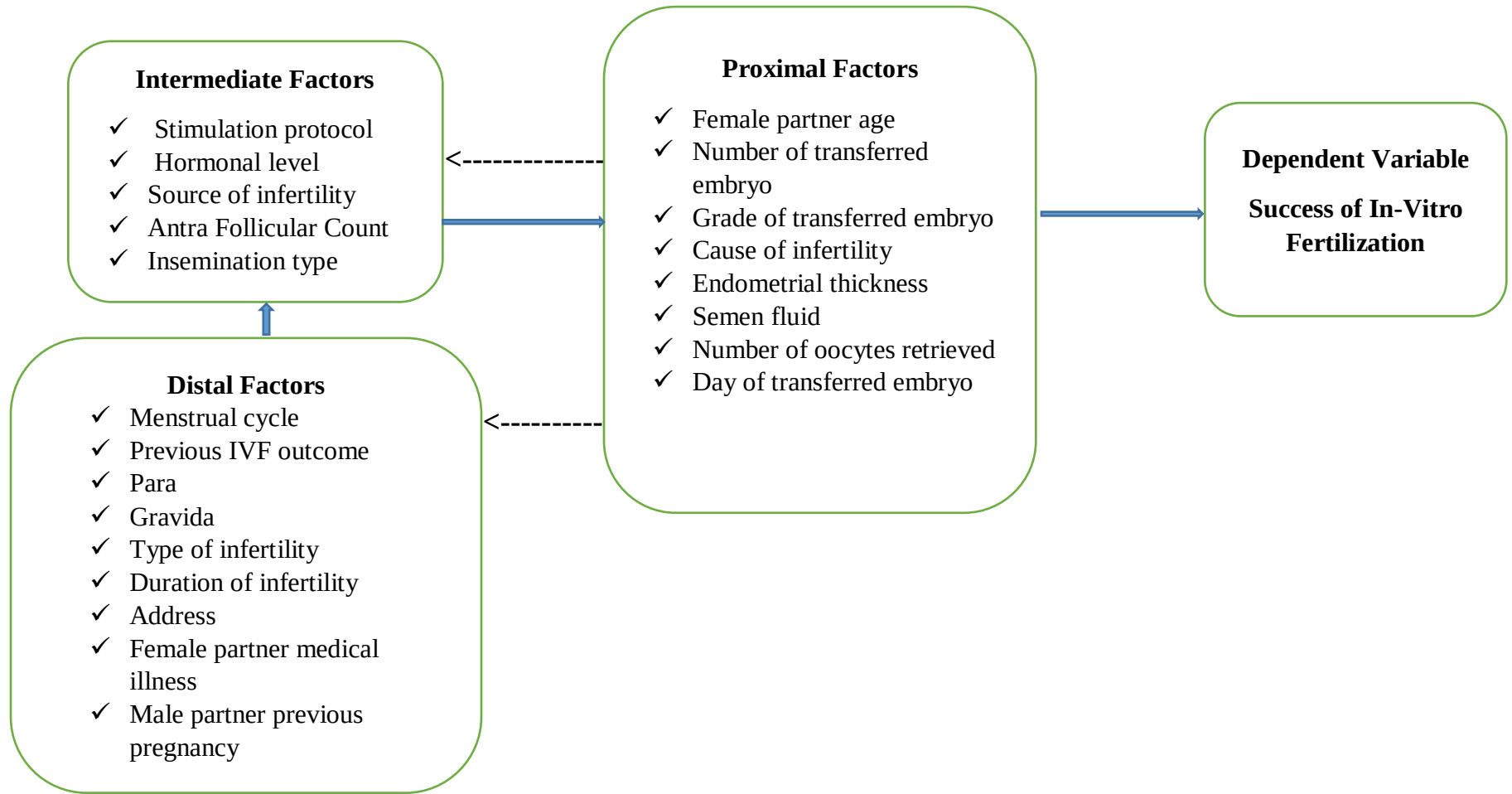


Figure 1 Conceptual framework on associated factors of success of IVF, in CFRM, Addis Ababa, Ethiopia, 2023 (11,21,23,50,54,55)

3. Research Objectives

3.1. General objective:

This study aimed to assess the magnitude of IVF success and associated factors among couples treated in Center for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia 2023.

3.2. Specific Objective:

1. To determine magnitude of IVF success among couples treated in Center for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia 2023.
2. To identify associated factors of IVF success among couples treated in Center for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia 2023.

4. Methodology

4.1. Study Setting and Period

The study were conducted from February 1 to March 30, `2023 in Center for Fertility and Reproductive Medicine (CFRM), which is a fertility treatment center under St. Paul's Hospital Millennium Medical College (SPHMMC) in Addis Ababa, Ethiopia. The center also called Michu Clinic, St.Paul's Fertility Center. In Addis Ababa, the capital city of Ethiopia, there are four infertility treatment centers; the pioneer was Alhikmah Clinic at Bole, next was CFRM, followed by New Leaf clinic, found around Sarbet, and Ethio life at Torhayloch. The CFRM was the first public fertility center in Ethiopia under SPHMMC Department of Obstetrics and Gynecology and it was found around Hayahulet, Addis, Ababa, Ethiopia. The hospital started IVF treatment in February 2019. Accordingly, until September 2023 more than 37,592 infertile couples were evaluated and IVF conducted for more than 3664 couples which makes it 70-90 IVF per month (11). On September 2021 to 2022, a total of 1281 IVF (1164 fresh egg and 117 frozen egg transfer) conducted and from September 1, 22 to August 31, 23 there were 1164 IVF/ICSI conducted.

4.2. Study Design

An institution-based retrospective record review was conducted.

4.3. Populations

4.3.1. Target Population

All infertile couples who had IVF treatment in CFRM, Addis Ababa, Ethiopia

4.3.2. Source and study population

All infertile couples who had IVF treatment between September 1, 22 to August 31, 23 in the Centre for Fertility and Reproductive Medicine and fulfilled the inclusion criteria.

4.3.3. Study Units

IVF treated infertile couples during the study period

4.3.4. Sampling Frame

Is the list of IVF treated infertile couples during the study period.

4.4. Eligibility Criteria

4.4.1 Inclusion Criteria

All infertile couples who had IVF treatment in CFRM during period September 1, 2022 to August 31, 2023.

4.4.2. Exclusion Criteria

Incomplete records were excluded from the study.

4.5. Sample Size Determination and Sampling Technique

4.5.1. Sample Size Determination

All clients data, 1164 for a full year September 1, 22 to August 31, 23, (which was above the projected sample size in table 1), was analyzed.

Table 1 Summary of sample size calculation based on the research objectives, CFRM, SPHMMC, Addis Ababa, Ethiopia, 2023

Sample size determination based on objective one;							
- Single Population Proportion Formula. Sample Size $(N) = \frac{(Z \alpha/2)^2 pq}{(d)^2}$ - Assumptions: Margin of error (d) = 4%, Level of significance (α)=0.05, Confidence Interval (CI) = 95%, Z= 1.96 Non response 10%							
$\Rightarrow$ magnitude of success of IVF (P) = 30% (0.3) (11) $\Rightarrow$ q= 1-P = 1-0.3= 0.7		$\frac{(1.96)^2 (0.3 \times 0.7)}{(0.04)^2} = \underline{504.2}$			N= 504.2 x 10%= 50.4 <u>N= 554.6 ~ 555</u>		
Sample size determination based on objective two; variables considered age, oocytes retrieved, and day embryo transfer							
- Double population proportion formula $(N) = \frac{(Z \alpha/2)^2 (p1q1+P2q2)}{(d)^2}$ - Assumptions: Confidence Interval (CI) = 95%, Power (P)= 80% , ratio, and odds ratio based on previous study conducted in the study site (11)							
Variable	% outcome exposed	% outcome unexposed	Ratio	Power	AOR	Non response rate	Maximum Sample size
Female partner age	53.4%	74.6%	1.48	80%	0.39	10%	196
Oocytes retrieved	83%	93.3%	2.82		0.35		454
Day 5 embryo	94.2%	83.3%	1.64		3.28		357

4.5.2. Sampling Technique

Data were collected from all couples who used IVF at CFRM within the study period.

4.6. Study Variables

Dependent Variable: Success of In-Vitro Fertilization

Independent Variables

- Demographic variables: female partner age, Address
- Clinical variables: cause of infertility, source of infertility, type of infertility, duration of infertility, menstrual cycle
- Procedure-related variables: stimulation protocol, number of embryos transferred, grade of transferred embryo, number of oocytes retrieved, previous IVF and outcome, insemination method, endometrial thickness and antra follicular count
- Hormonal level; AMH, TSH, day 3 FSH, day 3 LH, level of Estrogen hormone, prolactin hormone and
- Semen fluid

4.7. Operational Definitions

1. Successful IVF: in this study, the success of IVF was measured after recent IVF/IVF-ICSI treatment ultrasound result was viable fetus (11).
2. Unsuccessful IVF: unsuccessful IVF was, after recent IVF/IVF-ICSI treatment, ultrasound result was nonviable fetus (11)
3. Oocyte retrieved: (11)
Good responders: ≥ 4 oocyte retrieved
Poor responders: < 4 oocyte retrieved
4. Grade of embryo: In this study embryo day 3 and 5 both graded as 1, 2, 3 as per European Society of Human Reproduction and Embryology grading system. Grade 1: Good, Grade 2: Fair, Grade 3: Poor (56).
5. Source of infertility: person responsible for the cause of infertility
6. Address(57)
Urban: All administrative capitals, including those in each region, zone, and district.
Places with 2000 or more residents
Rural: Community with fewer than 2,000 residents. Places with 2,000 or more residents where the majority work primarily in agriculture
7. Couples: in this study couples refer those who are married

Standard Definitions

1. Semen Analysis (58).

I. Normal : semen volume ≥ 2 , sperm concentration ($10^6/\text{ml}/\text{total number}$, $10^6/\text{ejaculate}$) $\geq 20/\geq 40$, sperm motility (%) $\geq 50/\geq 25$, normal forms (%) ≥ 30

II. Abnormal:

- ✓ Oligozoospermia: sperm concentration lower than $15 \times 10^6 \text{ ml}^{-1}$
- ✓ Asthenozoospermia: sperm total motility lower than 40% or progressive motility lower than 32%
- ✓ Teratozoospermia: normal forms lower than 4%
- ✓ Oligoasthenoteratozoospermia or a combination of these three

2. Egg maturity: (59)

I. Metaphase (M2): Mature embryo

II. Metaphase (M1): Immature embryo, the egg was in the first phase of meiosis but not entered the second phase of meiosis and are on progress to maturity

III. Germinal Vesicle: Immature embryo, the egg has not begun meiosis.

IV. No egg retrieved: no egg found in the follicles

3. Embryo maturity:(56)

I. Grade 1: cells are of equal size; no fragmentation seen (good grade)

II. Grade 2: cells are of equal size; minor fragmentation only (moderate grade)

III. Grade 3: cells are of unequal size; no fragmentation to moderate fragmentation (low grade)

4. Serum HCG pregnancy test:

Pregnancy positive: >25 HCG level in blood

Pregnancy negative: <25 HCG level in blood

5. Gravida: Number of pregnancy

6. Para: Number of birth of viable fetus

7. Menstrual cycle

Normal: are regular menstrual cycle with 28 days cycle, 4-7 days intervals,

Abnormal: include irregular menses, which occur fewer than 21 days or more than 35 days, light or heavy bleeding, OR Absent menses, missing three or more periods

8. Infertility: Failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse (60)

9. Number of retrieved oocytes: (56)

Poor responders: retrieved oocytes < 4

Good responders: retrieved oocytes > 4

10. Miscarriage: is a spontaneous loss of pregnancy before 20week of gestation or expulsion of a fetus or embryo weighing 500 g or less.

4.8. Data Collection Tool and Procedure

A structured and pretested English version questionnaire adopted from previous studies was used to collect data from client's electronic chart. The questionnaire consists of seven parts: demographic characteristics including, female partner age and address. Second, clinical characteristics, history of medical illness, menstrual cycle, gravida, para, history of miscarriage, cause of infertility, source of infertility, infertility type, duration of infertility. Third, questions related to female hormonal level, level of prolactin hormone, day three LH, AMH, TSH, day three FSH, level of Estrogen, and endometrial thickness. Fourth, quantity and grade of transferred embryo. Fifth, semen analysis and six, procedure related factors including stimulation protocol, type of insemination, retrieved oocytes, AFC, previous IVF and outcome.

Data collector was one female health professional who had a masters degree in reproductive health were used.

4.9. Data Quality Control

Structured English version questionnaire was adopted from previous studies were used to collect data from client's electronic chart. In order to assess the appearance of the questionnaire in terms of feasibility, consistency, formatting, and the clarity of the language, before the actual data collection, pretest of the questionnaire was carried out on 59(5%) couples from the year 2021 and amendments was conducted accordingly. From client's electronic registration list, clients who underwent IVF in the study period identified and data collected from the client's electronic charts. Couples electronic charts were registered on computer system called Electronic Medical Record database. Moreover, for prevention of missing data, on variables that was not found on clients electronic chart, data searched on their scanned medical records.

Data was collected by a health professional using structured questionnaire developed on KOBO toolbox and the researcher conducted supervision. The data collector received a three-days training

to become familiar with the objective of the study, questionnaire type and content, Electronic Medical Record database content, Kobo toolbox, and data collection and submission technique. Collected data were checked daily for completeness and consistency on the excel and regular communication was carried out in order to identify and solve problems on time. Data was collected electronically using mobile data collection tool (Kobo toolbox), which maintained the data collection quality.

4.10. Data Management, Processing, and Analysis

The data were routinely collected in the facility for clinical monitoring and evaluation purposes and captured in the patient electronic chart. The Gynecologists, reproductive endocrinology and embryologist, and other health personnel working in the fertility clinic recorded the data. The data was extracted and recorded in the Kobo mobile application, exported to Microsoft Excel, then to Statistical Package of Social Science (SPSS) version 26. Data were checked for inconsistencies, completeness, and cleaned on SPSS. Through complete case-wise deletion, all observations that contain missing data were removed, and only complete observations were considered for final statistical calculations. The analysis was conducted using SPSS version 26. The patient characteristics were described in terms of frequencies, mean, median, or percentage, as appropriate.

Logistic regression was used to determine predictors of success of in-vitro fertilization, odds ratios (OR) with 95% confidence intervals (CI). Variables with $p < 0.25$ in bivariate logistic regression was transferred to multivariable logistic regression to control possible confounders. Statistical significance was declared at $p\text{-value} < 0.05$. Tables and figures was used to present the findings. The assumption of logistic regression was checked on Hosmer-Lemeshow goodness of-fit-test. The internal consistency of the data was checked with Cronbach's alpha.

4.11. Ethical Consideration

Ethical clearance was obtained from the Ethical Review Board of SPHMMC and permission was offered from chief executive officer of CFRM. Given the secondary nature of the data, participants consent was waived. Confidentiality of data was kept in each step. The personal identification of participants was not included rather patient record number was utilized.

5. Results

5.1. Demographic and Clinical Characteristics of Participants

In a period of one year, from September 1, 22 to August 31, 23, 1164 couples had undergone IVF treatment in CFRM. In this research, a total of 924 couples participated, and in the analysis, 22 variables were assessed and finally, the association of IVF success with 18 variables were evaluated.

Table 2 lists the number and frequency of the variables for both successful and unsuccessful deliveries. Majority of female partner age was < 35, 599 (64.8%) and the age ranges from 21- 49 with a mean age 33.3 ± 5.1 SD. Majority of participants resided in urban area 705 (76.3%) and out of this 565 (61%), are from Addis Ababa (see table 2). One of the eligibility criteria for IVF was marriage certification, thus, all 924 (100%) of couples in this study were married in status and couples were obliged to obtain legal marriage certification for confirmation.

According to the clinical findings, those with normal or regular menstrual cycle accounted to be 816 (88.3%). Whereas abnormal menstrual cycle accounts 108 (11.7%) of this irregular menses is 97 (10.5%), and absent mensus accounts 11(1.2%). Among the participants, 619 (67%) had primary infertility. Out of women who had previous pregnancies, 792 (85.7%) had no viable fetus. Moreover, over half of couples had infertility duration >5, 513 (55.5%). The period of infertility ranges from 1 to 24 year, with median duration 6 year, and IQR 6years. Majority (93.5%) of male partner had no previous pregnancy (see the detail in table 2).

Table 2 Demographic and Clinical Characteristics of Participants in Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023 (n=924)

Variables	Variables category	Number(N)	Percent (%)
Female partner age	<35	599	64.8
	>35	325	35.2
Address	Urban	705	76.32
	Rural	219	23.7
Menstrual cycle	Normal	816	88.3
	Abnormal	108	11.7
Type of Infertility	Primary	619	67
	Secondary	305	33
Duration of infertility	<5	411	44.5
	>5	513	55.5
Female medical illness	No	764	82.7
	yes	160	17.3

Medical illness type	Diabetes Mellitus	110	68.75
	Hypertensive	29	18
	Other**	21	13
Source of infertility	Combined factor	110	11.9
	Female factor	553	59.8
	Male factor	125	13.5
	unidentified	136	14.7
Semen Fluid	Normal	674	72.9
	Abnormal	250	27.1
Gravida	0	619	67
	≥ 1	305	33
Para	0	792	85.7
	≥ 1	132	14.3
History of miscarriage	No	213	23
	Yes	92	10
Retrieved oocytes	>10	185	20
	<10	739	80
Previous pregnancy male partner	No	864	93.5
	Yes	60	6.5

Other**: Thyroid disease and HIV

5.2. Female and male cause of infertility

In this research, female infertility cause was the main contributor to infertility, accounts for 553 (59.8%) of cases. Infertility due to male factor was the second most cause, affecting 125 (13.5%) of cases. And rest was combination factors 110 (11.9%) and unknown cause 136 (14.7%) (table 2). The major cause of female infertility was tubal blockage 346(62.6%) followed by uterine mass and ovarian cyst (see figure 2). In addition, major male cause of infertility was Oligoasthenoteratospermia 92 (73.6%), followed by Oligozoospermia 19(15.2%) and Asthenozoospermia was 14(11.2%).

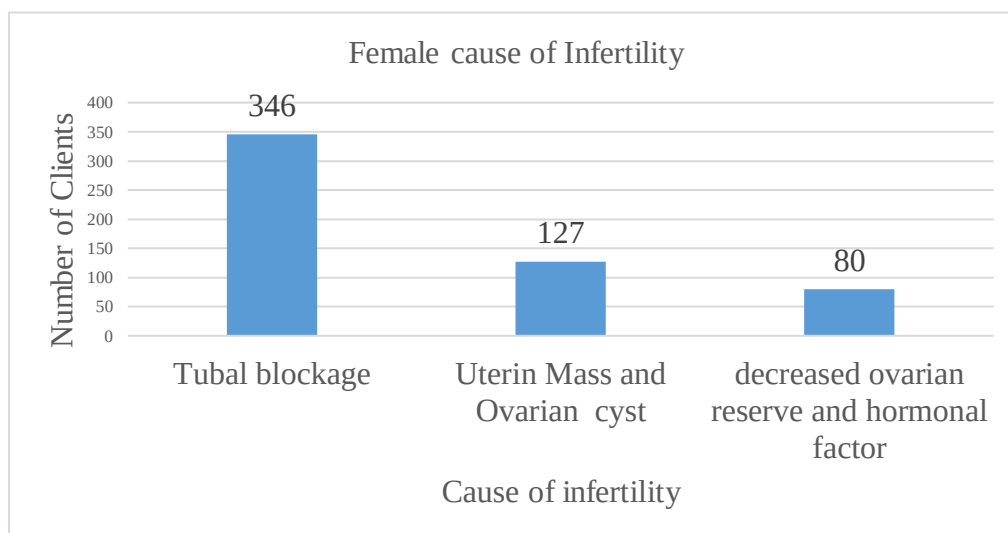


Figure 2 female cause of infertility, in Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023 (n=553)

5.3. Hormonal level and endometrial thickness

Of the total, 547 (59.2%) of the participant's endometrial thickness was > 7 , with mean of 7.03 SD ± 3.2 . Moreover, 57% had abnormal FSH level and of tested 18 % had abnormal AMH, indicating ovarian reserve might be compromised. Additionally, only 16.7% had normal LH, those with low and high LH 132 (13.6%) might have compromised ovarian reserve. Those with normal TSH 455(49.2%) has positive embryo implantation. In addition, normal level of prolactin hormone 550 (59.5%) related with regular ovulation (See table 3).

Table 3 Hormonal level of participants in Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023 (n=924)

Variable	Variables category	Number (N)	Percent (%)
Endometrial thickness	>7	547	59.2
	<7	377	40.8
Follicle Stimulating Hormone	Normal	397	43
	Abnormal	527	57
Luteinizing Hormone	Normal	154	16.7
	Abnormal	132	13.6
	unknown	645	69.7
Anti Mullerian Hormone	Normal	62	6.7
	Abnormal	194	18
	unknown	696	75.3
Prolactin Hormone	Normal	550	59.5
	unknown	374	40.5
Thyroid Stimulating Hormone	Normal	455	49.2
	Abnormal	45	4.9
	unknown	424	45.9

Note: hormonal level at reproductive age: FSH Normal: 0.1-22.2MIU/ml Abnormal * <0.1 and >22.2 , and unknown

:LH Normal: 5-25IU/L

Abnormal** <2 and >25

: AMH Normal 1.0ng/ml-3.0ng/ml

Abnormal*** Low (<1.0 ng/ml) and High (>3 ng/ml)

: Prolactin Normal 0.052ng/ml-465.3

Abnormal <0.052 and >465.3

: TSH Normal 0.35-4.94 MIU/L

Abnormal < 0.35 and > 4.94

5.4. Procedure related factors and prior IVF outcome

Majority of cycles used minimal stimulation protocol 442 (47.8%) which uses a limited amount of fertility drugs to produce high-quality eggs. Moreover, IVF-ICSI was a more practiced procedure than conventional IVF. The research finding reported that number of antra follicular counts ranges from 0 to 40 with a mean value of 10.2 SD ± 8.8 and the majority (75.4%) of clients had > 5 antra

follicular counts which indicates positive IVF outcome. Furthermore, among females who had previous IVF 228 (24.7%), 63 (17.8%) had successful IVF (see table 4).

Table 4 procedural and prior IVF related factors in Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023 (n=924)

Variables	Variables category	Number (N)	Percent (%)
Simulation protocol	minimal	442	47.8
	short	282	30.5
	long	200	21.6
Day Transferred Embryo	Day 3	695	75.2
	Day 5	229	24.8
	>1	685	74.2
Number Embryo Transfer	1	159	17.2
	unfertilized	80	8.7
Grade embryo transferred	Grade 1	612	66.2
	Grade 1, 2	194	21
	Other*	118	12.8
Insemination type	IVF-ICSI	562	60.8
	Conventional IVF	362	39.2
Antra Follicular Count	>5	697	75.4
	<5	227	24.6
Previous IVF	Yes	228	24.7
	No	696	75.3
Prior IVF outcome	successful	165	17.9
	Not successful	63	6.8
Number Retrieved Oocytes	>4	545	59
	<4	379	41
Cause of infertility	Known	425	46
	Unknown	499	54

Other ; grade 1,2,3 AND Grade 1,3 AND Grade 2,3 and grade 3*

5.5. Success of IVF and Cause of unsuccessful IVF

This research identified that 321 (34.7%) of couples had successful IVF in CFRM, Addis Ababa, Ethiopia (figure 3). IVF success based on serum HCG level > 25 or by chemical confirmation was 352 (38.2%) (see figure 4). However, the result reduced to 321 (34.7%) on the clinical confirmation (see figure 3).

The major cause of unsuccessful IVF was unidentified 499 (82.7%) and no fertilization accounted 58 (9.62%), and 46 (7.68%) was for endometrial abnormality or fundal scar.

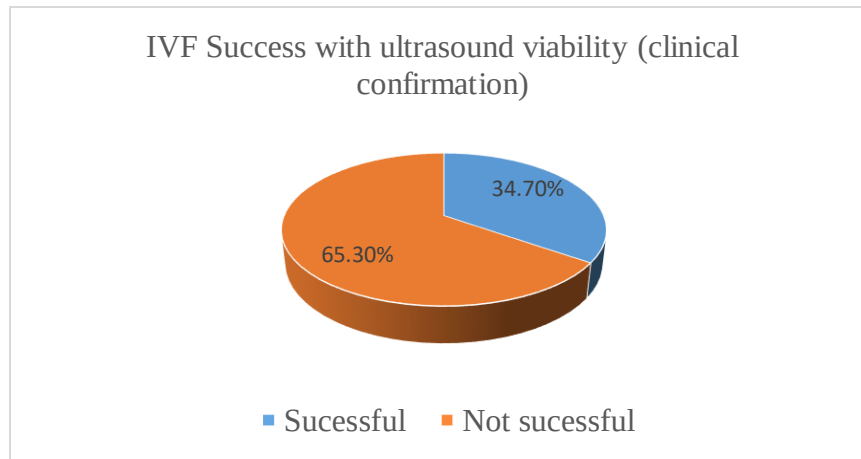


Figure 3 Success of in vitro fertilization based on clinical confirmation in the Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023

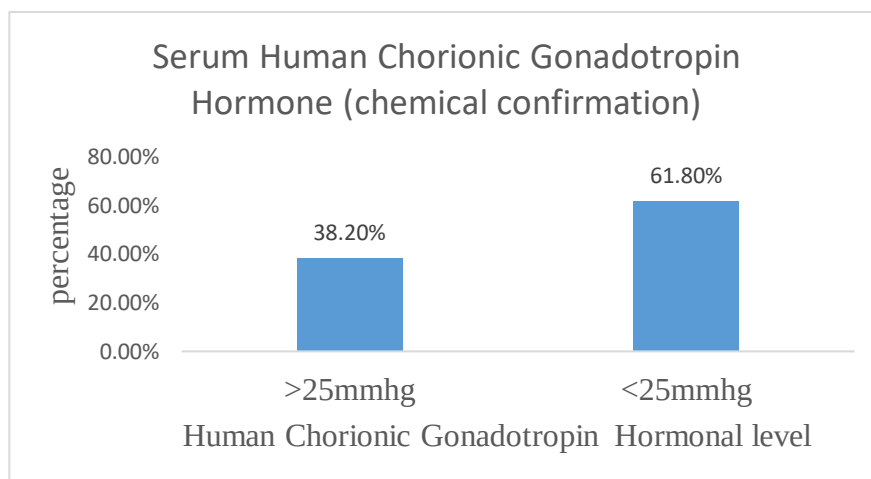


Figure 4 Success of in vitro fertilization based on chemical confirmation in the Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023

5.7. Factors associated with the success of IVF

Bivariate logistic regression was conducted to see the association of each single independent variable with the dependent variable. The analysis result showed that, nine variables were significant with p value <0.25. These are female partner age >35 (COR 0.32, 95% CI: 0.231-0.437 p=0.001), duration of infertility $\leq$ 5 years, (COR 1.55 95% CI: 1.14-2.112, p=0.006), female medical illness, (COR 0.69 95% CI: 0.46-1.06, P=0.089), para zero, (COR 0.34, 95% CI: 0.16-0.71, p=0.004), history of miscarriage, (COR 1.80 95% CI: 0.58-1.92, p= 0.19), number of

retrieved oocytes ≤ 4 , (COR 0.76 95% CI 0.53-1.08, $p=0.13$), stimulation protocol long, (COR 0.69 95% CI 0.46-1.05 $P= 0.08$), stimulation protocol short, (COR 0.94 95% CI 0.64-1.36 $P= 0.73$), Day 3 embryo transfer (COR 0.28, 95% CI: 0.19-0.39, $p<0.001$), and antra follicular count <5 (COR 0.56 95% CI 0.36-0.89, $p= 0.01$) were associated with success of IVF (see table 5). Following bivariate analysis, to control for the confounder effect, multivariable logistic regression was conducted by inserting variables with p value < 0.25 on the bivariate analysis.

As shown in Table 5, on the multivariable logistic regression, the analysis revealed that, female partner age > 35 years (AOR 0.52, 95% CI 0.36-0.75, $p<0.001$), duration of infertility ≤ 5 years (AOR 1.57, 95% CI 1.16-2.13, $p=0.006$), number of retrieved oocytes ≤ 4 (AOR 0.70, 95% CI 0.50-0.99, $p= 0.04$), day 3 embryo transfer (AOR, 0.29 95% CI 0.20-0.41, $p<0.001$), and antra follicular count < 5 (AOR, 0.55, 95% CI 0.35-0.85, $p=0.007$) were associated with success of in vitro fertilization (see table 5).

Table 5 Bivariate and multivariable regression analysis, in Centre for Fertility and Reproductive Medicine, SPHMMC, Addis Ababa, Ethiopia, 2023 (n=924)

Variables	Variables Category	IVF Unsuccessful	IVF successful	P-Value	COR	95% CI		P value	AOR	95% CI	
						Lower	Upper			Lower	Upper
Female partner age	>35	262	63	0.001*	0.318	0.231	0.437	0.000**	0.523	0.364	0.752
	≤35	341	258	1	1	1	1	1	1	1	1
Menstrual cycle	Abnormal	78	30	0.267	1.360	0.817	2.262				
	Normal	525	291	1	1	1	1				
Type of infertility	Secondary	212	93	0.570	0.647	0.145	2.898				
	Primary	391	228	1	1	1	1				
Duration of infertility	≤5	244	167	0.006*	1.549	1.135	2.114	0.004**	1.572	1.158	2.132
	>5	359	154	1	1	1	1	1			
Female medical illness	Yes	116	44	0.089*	0.695	0.457	1.057	0.056	0.90	0.890	2.272
	No	487	277	1	1	1	1	1	1	1	1
Source infertility	Combined female male factor	68	42	0.872	0.946	0.483	1.852				
	Male factor	67	58	0.269	1.284	0.824	2.002				
	Unidentified	86	50	0.494	0.791	0.405	1.546				
	Female factor	382	171	1	1	1	1				
Semen analysis	Normal	147	103	0.822	1.058	0.648	1.729				
	Abnormal	456	218	1	1	1	1				
Gravida	0	389	230	0.408	1.846	0.432	7.894				
	≥1	210	95	1	1	1	1				
Para	0	516	276	0.004*	0.338	0.160	0.712	0.118	0.704	0.453	1.094
	≥1	87	45	1	1	1	1	1	1	1	1
History of miscarriage	Yes	147	66	0.190*	1.803	0.578	1.915	0.743	1.066	0.729	1.557
	No	456	255	1	1	1	1	1	1	1	1
Number of retrieved Ocytes	≤4	290	89	0.129*	0.760	0.534	1.083	0.042**	0.703	0.501	0.987
	>4	313	232	1	1	1	1	1	1	1	1
Previous pregnancy male partner	No	556	308	0.330	0.692	0.329	1.452				
	Yes	47	13	1							
Endometrial thickness	≤7	244	134	0.858	0.972	0.710	1.330				
	>7	359	187	1							
Stimulation Protocol	Long	92	108	0.082*	0.692	0.457	1.048	0.056	1.490	0.990	2.241
	Short	180	102	0.730	0.936	0.642	1.363	0.718	1.070	0.741	1.544
	Minimal	331	111	1	1	1	1	1	1	1	1
Day of embryo transfer	Day 3	521	174	0.000*	0.277	0.192	0.399	0.000**	0.286	0.201	0.407
	Day 5	82	147	1	1	1	1	1	1	1	1
Transferred Embryo Grade	Grade 1,2	110	84	0.26	1.472	1.059	2.047				
	Other*	90	28	0.28	0.60	0.380	0.946				
	Grade 1	403	209	1	1	1	1				
IVF insemination	Conventional IVF	241	121	0.986	1.003	0.913	1.333				
	IVF-ICSI	362	200	1	1	1	1				
Antra Follicular Count	<5	193	34	0.013*	0.564	0.359	0.887	0.007**	0.545	0.349	0.849
	>5	410	287	1	1	1	1	1	1	1	1

*P value <0.25 **P Value <0.05 Other* ; grade 2, grade 1,2,3 AND Grade 1,3 AND Grade 2

6. Discussions

This study assessed the magnitude and associated factors to success of IVF in the CFRM and it was found that, female age, duration of infertility, day of embryo transfer, retrieved oocytes, and antra follicular count were significant predictors for the success of IVF. Whereas; IVF stimulation protocol, menstrual cycle, day of transfer, embryo grade, gravida, medical illness, and parity were not significantly associated with success of IVF with P value >0.05 .

In this study, 321 (34.7%), (95% CI 32.0-36.0) had successful IVF. This finding is in line with the global IVF success rate which is 30% (10) and a 2019 study conducted in Ethiopia, which reported 30.1% (11). However, the finding was below the IVF success found in Iran which was 81.2% (21). And higher comparing to studies conducted in developed countries, in America 19.2% (31) and in Brazil 0.4% (30). Reason for disparities might be due to difference on technological service, service accessibility, and treatment cost.

This study found that couples with a shorter duration of infertility (≤ 5 years) had higher likelihood of achieving a success pregnancy after IVF compared to those with longer duration (>5 years) with an adjusted odds ratio of 1.57 (95% CI 1.158-2.132, $p=0.004$). Result indicated, couples with shorter infertility had approximately 1.57 times higher odds of IVF success than there counterpart. This is consistent with previous research, short duration of infertility is 2.1 (95%,CI 1.32-2.85 $P=0.006$) times high likelihood of IVF success (21), whereas, higher duration of infertility is 0.61 times (AOR 0.61, 95% CI 0.42-0.86, $P = 0.006$) (37) and 0.9 (AOR, 0.91; 95% CI, 0.72-1.15) times lower odds of IVF success (36). Longer duration likely reflects declining ovarian reserve and poorer oocyte quality over time. Prolonged inflammatory and immunological changes in the reproductive tract may also hinder implantation after longer infertility(37). The findings confirm duration of infertility as an independent prognostic factor for IVF success. The 5-year cutoff identified provides a clinically useful benchmark to counsel patients regarding their chances of success. However, the causes underlying infertility duration need to be considered.

This study showed that, compared to retrieval of four or more oocytes, extraction of less than four oocytes was substantially related with decreased likelihood of a successful IVF. As compared to retrieval of four or more oocytes, retrieval of less than four oocytes was associated with an adjusted

odds ratio (AOR) of 0.703 (95% CI 0.501-0.987, $p=0.04$). The likelihood of IVF success is 0.7 times decreases, when the number of retrieved oocytes falls below four. According to European Society of Human Reproduction and Embryology guideline, the adequate number of retrieved oocyte ranges from Five to Ten and below this number might relate with poor quality of the oocytes (56).

The day of embryo transfer was significantly associated with IVF success. Compared to day 5 transfer, day 3 embryo transfer had an lower odds of IVF success with an adjusted odds ratio (AOR) of 0.29 (95% CI 0.201-0.407, $p0.001$) for IVF success. This shows that cleavage stage embryo transfer on day three was 71% less likely to result in a successful IVF cycle than blastocyst transfer on day five. The finding is consistent with other study, Day 5 embryo transfer were 3.28 (95% CI 1.42-7.62 $P=0.006$) times high likelihood of IVF success than day 3 embryo transfer (11). The result was also in line with the body of research showing that transferring embryos at the blastocyst stage on day 5 leads to greater success of IVF than transferring embryos at the early cleavage stage on day 3. This is due to the higher probability of day 5 implantation rate (45).

In this study, lower Antra Follicular Count was significantly associated with reduced likelihood of successful IVF. Women with Antra Follicular Count ≤ 5 had approximately half the odds of IVF success compared to those with higher ovarian reserve (>5 follicles), with an AOR of 0.54 (95% CI 0.34-0.84, $p=0.007$). These results are consistent with prior study in Ethiopia that showed, < 5 Antra Follicular Count was an important predictor of IVF success with AOR 0.34 (95% CI 0.04-0.94, $P=0.33$) (11). Antra Follicular Count reflects the collection of follicles and ovarian reserve. The threshold of 5 follicles revealed in this analysis was significant, as prior studies reported similar Antra Follicular Count cut-offs indicating poor response, indicating that low Antra Follicular Count signifies reduced oocyte production and diminished embryo quality, which affects IVF success (6,28). Diminished ovarian reserve limits availability of good quality embryos after ovarian stimulation. Embryos from low Antra Follicular Count cycles may have higher chromosomal abnormalities and lower implantation potential (28). Patients should be made aware of the decreased possibilities even though pregnancy can still happen with a low Antra Follicular Count. More study was required to optimize egg quality and improve recruitment in these women (11).

It was confirmed that there was a reverse association between older female age and IVF success. Female partner aged over 35 was associated with 0.5 times reduced odds of IVF success compared to age under 35 (AOR 0.523, 95% CI 0.364-0.752, $p < 0.001$). Those younger females age (<35 years) had an increased likelihood of having a successful pregnancy following IVF. Women under 35 had around twice the odds of IVF success compared to older women. This result is consistent with prior evidence in Ethiopia, that advanced female age >35 negatively impacts IVF outcomes with (AOR 0.39, 95% CI 0.18-0.83, $p = 0.015$) (11) and in Brazil where < 35 age was higher chance of IVF success with (AOR 15, 95% CI 5.9-41.6, $P < 0.001$)(30) and a retrospective study female age (AOR 0.87, 95% CI 0.78-0.95) ($P = 0.008$) (37). Studies reported that Ovarian reserve and oocyte quality decline with aging, reducing number and quality of embryos available for transfer (22,61). Older women also have higher rates of chromosomal abnormalities leading to lower implantation and higher miscarriage rates after IVF. These studies provided further confirmation that female age was a key predictive factor for IVF success. Age 35 appears to be an important threshold, showing marked reduction in IVF success beyond this age (22,25). Earlier IVF treatment in younger women may help improve cumulative outcomes.

In this study, it was discovered that women's with medical illnesses showed a lower likelihood of achieving successful pregnancy after IVF compared to women without illnesses. The AOR 0.9, 95% CI 0.89-2.27, $p = 0.05$). Indicating women without medical conditions had approximately 0.9 times lower odds of IVF success. These results were in line with previous studies indicating reduced IVF success rates among women with medical comorbidities like diabetes, autoimmune disorders, and thyroid dysfunction (41). However, the CI crossed 1, the association might not be reliable.

In conclusion, the findings of this study and other research on IVF were in agreement that factors affecting IVF success include the age of the female partner, the number of antra follicles, and the duration of infertility. However, major expected variables like semen analysis and grade of transferred embryo doesn't shown any significance.

7. Strength and Limitation

This study tried to address maximum sample size and number of independent variables. However, the study was conducted in one institution which limits the generalizability, due to the retrospective nature of the study, missed variables i.e hormonal levels, body mass index and male partner age were not assessed.

8. Conclusion

The study result showed that 34.7% of couples had successful IVF leading to a viable pregnancy. Key factors that were independently predictive of higher IVF success rates included higher antra follicular count, younger female age, shorter duration of infertility, >4 retrieved oocytes, and day 5 embryo transfer. The IVF stimulation protocol, menstrual cycle regularity, embryo grade, gravidity, and parity were not significantly associated with the success of IVF. Overall, these findings highlight important prognostic factors that can help identify couples with the highest chances of IVF success. Female age, antra follicular count, and day of embryo transfer appear to be particularly important, suggesting a role for individualized counseling and potentially tailored interventions in couples with advanced age or diminished ovarian reserve

9. Recommendation

Health Policymakers

- Can use the research finding to upgrade the IVF service and increase the success of IVF service.

Healthcare providers

- Should take into account female partner age, duration of infertility, follicular count, retrieved oocytes, and day of embryo transfer as a risk and take customized treatment plans into consideration.
- When providing patient counseling, organizing treatment regimens, and assessing IVF success rates, based on the female age will lead to better outcome
- Combining an evaluation of the duration of infertility with other variables, such as age and ovarian reserve, can help with patient selection and treatment choices in IVF.

Couples

- Couples should receive counseling on age-related effects in order to make good treatment decisions and expectations.
- Couples with shorter periods of infertility are encouraged to begin IVF earlier.

Researchers

- Researchers to carry out mixed studies that include other IVF facilities.

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11. Annex

Annex 1: Informed Sheet

My name was ----- am data collector and I am here on behalf of the investigator Mrs. Kidest Getu an Epidemiology student in St. Paul Hospital Millennium Medical College. This study was on Prevalence and Associated factors of In-Vitro Fertilization Success in this institution. Here below was a detailed information on the study to read and more, I will give you information about the research and ask for the institution's permission to participate and allow for data collection. Ahead before data collection, the institution delegate can ask and request any information and confirmation on the study.

Infertility was a global public health problem and the treatment options are limited and the success rate of the available treatment option are determined by different factors. It's known than In-Vitro Fertilization was the major Artificial Reproductive Technology option, which was also conducted in Centre for Reproductive Medicine, St. Paul Fertility Center. Therefore, this study aimed to assess the prevalence and associated factors for success of In-Vitro Fertilization. The result of this study will support health policy makers, concerned bodies, care providers to improve the service, and characterize infertile couples to increase the success of IVF.

This research uses clients chart to get information's needed. The data was collected using questioner. Engaging in this research was voluntarily. There was no negative impact/risk or right away benefit/incentive on participation and not participation. Participation can be discontinued at any point, however, this result will support the IVF procedure improvement and increase the success. Confidentiality of data was kept, participant's identification was not be requested, and rather the questioners was coded. Data only accessed by the data collectors and the researchers.

This research was supported, reviewed, and approved by St. Paul Millennium Medical College Ethical Review Board. If you need any further information or have any questions regarding this research, you can use the contact address below.

- Kidest Getu; 0913102382, kidestgetu2006@gmail.com

Annex 2: Research Questioner

S.no	Questions	Choice	Remark
PART 1: Demographic Questions			
101	Female partner age in year	_____	
102	Address	_____	
PART 2: Clinical Related Questions			
201	Women diagnosed with medical illness	1. yes 2. No	IF NO, SKIP TO QUESTION NUMBER 203
202	Women medical illness type	1. Diabetes melitus 2. Hypertensive disorder 3. Cardiac disease 4. Thyroid disease 5. Cancer 6. Other_____	
203	Menstrual cycle?	1.Regular 2.Irregular 3. Absent	
204.	Type of infertility	1. Primary 2. Secondary	IF ANSWER WAS PRIMARY INFERTILITY SKIP TO QUESTION NUMBER 208
205.	Gravida	_____	
206.	Para	_____	
207	History of miscarriage	1. No 2. Yes	
208	Duration of infertility in years	_____	IN NUMBER
209	Source of infertility	1. Female factor 2. Male factor 3. Combined factor 4. Unidentified	IF MALE FACTOR, GO TO QUESTION NUMBER 212 IF UNIDENTIFIED GO TO QUESTION NUMBER 213
210	Cause of infertility, Female factor	1. Endometriosis 2. Tubal blockage 3. Decreased ovarian reserve 4. Congenital anomaly 5. Polycystic ovarian syndrome 6. Hormonal factors 7. Medical disease 8. Asherman syndrome 9. Mayoma/polyp	MULTIPLE ANSWERS WAS POSSIBLE

		10. Other _____ _____	
211	Previous pregnancy male partner	1. Yes 2. No	
212	Cause of Infertility, Male Factor	1. Oligozoospermia 2. Asthenozoospermia 3. Teratozoospermia 4. Oligoasthenoteratozoospermia 5. Other _____ _____	MULTIPLE ANSWERS WAS POSSIBLE
213	Semen Analysis	1. Normal 2. Abnormal	
PART 3: Hormonal Level and Endometrial thickness			
301	Level of prolactin hormone	_____	IF NOT CONDUCTED SKIP TO QUESTION NUMBER 302
302	Level of Anti Mullerian hormone	_____	IF NOT CONDUCTED SKIP TO QUESTION NUMBER 303
303	Level of Thyroid Stimulating Hormone	_____	IF NOT CONDUCTED SKIP TO QUESTION NUMBER 304
304	Day 3 Level of Follicle Stimulating Hormone	_____	IF NOT CONDUCTED SKIP TO QUESTION NUMBER 305
305	day 3 Level of Estrogen hormone	_____	IF NOT CONDUCTED SKIP TO QUESTION NUMBER 306
306	day 3 Level of Luteinizing Hormone	_____	IF NOT CONDUCTED SKIP TO QUESTION NUMBER 307
307.	Endometrial thickness	_____	
PART 4: Quantity and Grading of Utilized Egg and Transferred Embryo			
401.	Antra Follicular Count	_____	
402.	Number of retrieved oocytes	_____	
403.	Number of embryo transferred	1. Three 2. Two 3. One 4. Unfertilized	

404.	Day of embryo transfer	1. Day 5 2. Day 3	IF UNFERTILIZED, SKIP TO QUESTION NUMBER 506
405.	Transferred embryo grade	1. Grade 1 2. Grade 2 3. Grade 3	IF MORE THAN ONE EMBRYO WAS TRANSFERRED MULTIPLE ANSWER WAS POSSIBLE
Part 5: Procedure related questions			
501	Have you had IVF before	1. Yes 2. No	IF NO SKIP TO QUESTION NUMBER 505
502	Stimulation protocol	1. long/ agonist 2. Short/antagonist 3. Minimal 4. Natural	
503	Insemination method	1. Conventional IVF 2. IVF-ICSI	
504	Current IVF outcome	1. Successful 2. Unsuccessful	
505	Possible reason for unsuccessful IVF outcome	_____ _____	

Annex 3 Declaration

I the undersigned declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Master of public health in **Epidemiology**. I also declare that it has never been presented in this or any other higher institution and that all resources and materials used in the research work have been duly acknowledged.

Name of the student: Kidest Getu

Signature:  _____

Place of Submission: Addis Ababa

Date of Submission: _____

This thesis has been submitted with my approval as a College/University advisor.

Name of the primary advisor: Mr. Belayneh Lulseged

Signature: _____

Date: _____

Name of the co-advisor: Dr. Bizatu Mengistu

Signature:  _____

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