ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

SUCCESS RATES AND TIME-TO-LIVE BIRTH OF FERTILITY TREATMENTS AMONG COUPLES ATTENDING FERTILITY CENTERS IN ADDIS ABABA, ETHIOPIA

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I undersigned agree to accept all responsibilities for the scientific and ethical conduct of this research project and declare that this thesis is my original work in partial fulfillment of the requirement for the Master of Public Health in Epidemiology and Biostatistics

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APRROVAL BY EXAMINATION BOARD

This thesis by Saron Kasahun is accepted in its present form by the board of examiners as satisfying thesis requirements for the review of degree of masters of public health in Epidemiology and Biostatistics

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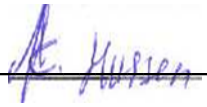
Date June 27, 2024 **Signature** 

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Saron Kasahun

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Abbreviations and Acronyms

AAU	Addis Ababa University
AFC	Antral follicular count
ANA	Antinuclear antibody
ART	Assisted reproductive technology
cIVF	Conventional In-vitro fertilization
CLBR	Cumulative live birth rate
COH	Controlled ovarian hyperstimulation
CPR	Cumulative pregnancy rate
EMT	Endometrial thickness
ET	Embryo transfer
ETB	Ethiopian Birr
HCG	Human chorionic Gonadotropin
ICSI	Intracytoplasmic sperm injection
IUI	Intrauterine insemination
IVF	In-vitro fertilization
LMIC	Low-and-middle income countries
PCOS	Polycystic ovary syndrome
PID	Pelvic inflammatory disease
PR	Clinical pregnancy rate
RH	Reproductive health
SPHMMC	St. Paul’s Hospital Millennium Medical College
STI	Sexually transmitted infection
USA	United States of America
WHO	World health organization

Abstract

Background: Despite impacting one in six individuals globally, infertility remains a neglected public health issue, particularly in low- and middle-income countries like Ethiopia. The emergence of local fertility centers offers promising alternatives to costly outgoing travel, crucial data on treatment success rates remains scarce.

Objective: To assess the treatment success rate and time to live birth of infertility treatments among couples attending public and private fertility centers in Addis Ababa, Ethiopia.

Methods: A cross-sectional study using data from patient chart was conducted among 411 couples from St. Paul's Hospital Millennium Medical College and Ethio fertility and IVF center in Addis Ababa. A simple random sampling technique was used to select samples from participants who started fertility treatments from March 2021 to February 2023. Data was collected by three nurses who work at the facilities using the data abstraction format and questionnaire under close supervision. Descriptive statistics and binary logistic regression analysis were used to assess the success rates of treatments in terms of clinical pregnancy, and Kaplan-Meier, Life Table, log-rank test and Cox regression were used to analyze the data on the time-to-live birth.

Results: Among the 411 couples who took fertility treatments, 47% and 33.1% were able to achieve clinical pregnancy and live birth, respectively. In-vitro fertilization has 39.3% success rate per cycle whereas, Intrauterine insemination registered 12% success per cycle. In terms of live birth, In-vitro fertilization procedure also achieved highest hazard of live birth compared to Intrauterine insemination. Woman's age ≥35, increased duration of infertility, and the presence of Tubal factor infertility were negative predictors of clinical pregnancy rate while, Antral follicle count ≥5, increase in number of treatment cycles, increase in endometrial thickness and increase in number of frozen cycle of IVF/ICSI indicated a higher chance of treatment success. Age ≥35, longer duration of infertility, frozen cycle type, AFC <5 and fewer number of treatment cycles had negative influence on live birth compared to their counter others.

Conclusion: Younger women and couples with repeated treatment cycles have better outcomes at clinical pregnancy and live birth. Assisted reproductive technology in Addis Ababa reach internationally comparable levels. Early intervention of infertility and repeated treatment cycles should be made available for all parts of Ethiopia and public awareness should be created.

Keywords: In-vitro fertilization, Clinical pregnancy, Assisted reproductive technology, Infertility, Live birth, Ethiopia

1. Introduction

1.1. Background

According to the international glossary on infertility and fertility care and the World health organization(WHO), infertility is defined as a disease that is characterized by the failure to establish a pregnancy after 12 months of regular, unprotected sexual intercourse (1,2) or due to an impairment of a person's capacity to reproduce, either as an individual or with his or her partner (3). It can be classified as primary or secondary. Primary infertility is where there is no previous conception, while secondary infertility is where the woman or couple already had one or more previous conceptions but failed at some point (4).

Several studies show that infertility is a widespread concern that is affecting large numbers of people all over the world (5). Approximately one in six people and around 17.5% of the adult population worldwide are struggling with infertility issues (6). In low- and middle-income countries (LMICs), infertility can present a challenge. For instance, it affects 25.1% of women in Iran and 30.7% in India (7,8). In the context of Africa, Sudan reported an overall infertility prevalence of 13%, predominantly with primary infertility (9). In Eritrea, male factor infertility has a prevalence of 42%, with primary infertility predominance (79.5%) (10).

Outgoing reproductive travel by citizens of various sub-Saharan African countries has been documented for treatments in the USA, Brazil, France, and destinations in the Middle East, including Dubai and Kuwait (13). Prior to the recent past, couples experiencing infertility would go outside of Ethiopia to receive medical care (14). The emergence of fertility centers in Ethiopia will reduce the travel people commonly make to Thailand, India, or South Africa for treatment, which offers a more cost-effective and convenient alternative to seeking treatment (14). However, the existing fertility centers are also located solely in Addis Ababa which may pose a great disadvantage for people living in peripheral sites. As these centers continue to evolve, their success rates in fertility treatments become crucial information to reshape the landscape of fertility care in Ethiopia, providing hope and solutions for the needy.

1.2. Statement of the problem

There is evidence highlighting a substantial burden of infertility worldwide, particularly in LMICs, across the African continent, notably in Ethiopia. The Ethiopian Demographic and Health Survey (EDHS) of 2016 indicated a high infertility prevalence of 24.2%, affecting more than one in five couples in the country (11). A 2021 study in Addis Ababa further emphasizes the significant burden, revealing an overall infertility prevalence of 27.6% (12).

Culturally, childbearing is highly valued in Africa, particularly in Ethiopia. Dominant religions in Africa and Ethiopia view children as blessings (15,16) and parenthood as a source of great fulfillment and personal completion for couples (17). This makes the inability to conceive emotionally devastating, potentially impacting psychological well-being significantly. Social stigma adds to the emotional burden. Beyond the biological and medical challenges, infertility carries a heavy social and emotional burden for couples in Ethiopia. They often face stigmatization, ridicule, and social pressure within their communities (18,19), compounding the already profound emotional struggles brought on by their inability to conceive.

It is the reproductive right of the couple to have access to fertility treatment options (20) and they should be able to have knowledge about the different aspects of outcomes related to the treatments. The determinants of fertility treatment success remain a multifaceted and under-explored domain in Ethiopia. Despite its importance, infertility prevention and care remain neglected public health issue (21). There are three major types of fertility treatments: medications, surgical treatment, and assisted reproductive technology (22). There is limited research and data on the success rates and time to success of the fertility treatments that are available in Ethiopia, even with the recent emergence of fertility centers in Addis Ababa. This limitation of crucial information impedes informed decision-making for both physicians and couples seeking treatment, potentially affecting the navigation of treatment options, financial planning, emotional preparation, and setting realistic expectations.

In conclusion, infertility in Ethiopia presents a complex and pressing issue with far-reaching consequences for couples facing it. Overcoming research and data gaps is a crucial step towards the advancement of fertility treatment and care in the country.

1.3. Rationale of the study

This study may address the existing gaps by systematically investigating the possible determinants of fertility treatment success and time to success. Knowing these factors and the direction of their effect may help health care practitioners and the couple undergoing such treatments. By shedding light on this, this study may identify the factors influencing the success and the time to live birth of the treatments, which is crucial for developing effective interventions, improving access to high-quality fertility care, and optimizing health care resources. The study could also provide insight for future research and guide the development of targeted interventions to improve treatment success rates and time to live birth .

This study evaluates the effectiveness of various infertility treatments, encompassing IVF, ICSI and IUI, across both public and private centers located in Addis Ababa. The assessment covered both fresh and frozen embryo transfers, evaluating outcomes in terms of clinical pregnancy and live births, considering multiple treatment cycles. Addressing these specific aspects is crucial, as previous studies conducted in Ethiopia had limitations in examining these evaluations. The present study could overcome these previous limitations and provide a more thorough understanding of the success rates in terms of clinical pregnancy and time to live birth associated with the different infertility treatments.

1.4. Significance of the study

Understanding the success rates and time to success of infertility treatments may inform healthcare policy and decision-making, resonating with the Reproductive Health (RH) strategy for Ethiopia (2021–2025). The RH strategy sets ambitious performance targets and major strategic initiatives to comprehensively address infertility, including upgrading diagnostic and management centers and initiating training programs. The results of this study could help evaluate the effectiveness of these targets, make informed decisions on future initiatives, and guide evidence-based policy decisions in the realm of infertility management, which in turn may have the potential to contribute to improved fertility care outcomes and enhance reproductive health services in Addis Ababa and across Ethiopia.

By assessing the treatment success rates of infertility, this study could provide couples with scientific evidence of how much chances of success they may have in Ethiopia to achieve

pregnancy and have their own babies. This may help the couple make informed choices, seek appropriate treatments, and manage their expectations.

2. Literature review

2.1. Epidemiology of infertility

For several societal and biological reasons, infertility is a significant public health and socioeconomic issue that can be resolved with early detection, prevention, and treatment (23). In a meta-analysis focused on the worldwide prevalence of infertility, the pooled prevalence of infertility among women was found to be 45.85%, and primary infertility was 51.5% (24).

Iran has an overall prevalence of infertility of 7.99% and a comparatively greater primary infertility than secondary infertility. The prevalence of infertility in Iran from (2000 –2010) to (2010 –2019) tended to increase with a slow slope, and urban areas had a greater prevalence than rural areas (25).

Africa ranked fourth in the prevalence of lifetime infertility with a prevalence of 9.3- 15.8% next to the Western Pacific region (8.2 –39.7%), regions of Americans (4.2 –35.3%), and Europe (9.0 – 31.8%), but ranked first in period infertility prevalence (9.5 –32.0%), from 1990 to 2021. Females had a higher period infertility prevalence than males (26). The prevalence of overall infertility was 13% in Sudan (9).

According to a study assessing the prevalence of primary and secondary infertility in Africa, North Africa (70.56%) and East Africa (30.37%) were found to have the highest and lowest proportions of primary infertility, respectively. In contrast, East (69.63%) and North Africa (29.58%) have the highest and lowest proportion of secondary infertility respectively. This high prevalence of secondary infertility can be accounted for by the high sexually transmitted infections (STIs), other infections followed by abortion, or the first pregnancy in these areas (27). Whereas, a low prevalence of secondary infertility was found in countries where the management of the above factors is relatively good (9,27). Female infertility accounted for 54.01% of the total infertility according to seven studies conducted in Africa, which makes it the highest type of infertility by factor of infertility. 22% was from male infertility, and the remaining was from an unknown cause (27). Also, another study done in Sudan found that 41% of infertility was due to female infertility and 27% was due to male factor infertility. The remaining accounted for combined and unexplained factors (9).

The causes of male infertility, starting with the most prevalent, were oligospermia, asthenozoospermia, and varicocele. For female infertility, pelvic inflammatory disease (PID), tubal factors, and abortion possess the highest rank, respectively (27). In Sudan, azoospermia and polycystic ovary syndrome (PCOS) were found to be the most common causes of infertility in males and females, respectively (9).

According to a study aimed to assess the prevalence of infertility in Ethiopia, 24.2% of the population suffers from infertility, and 90.7% of them are from secondary infertility (11). A study conducted in Addis Ababa showed the overall prevalence of infertility to be 27.6%. From this, the primary and secondary types of infertility are 14.4% and 13.2%, respectively (28). This shows the prevalence of infertility tends to be higher compared to studies done in the world and Africa.

2.2. Fertility treatment options and successes

Millions of people around the world have been helped by Assisted Reproductive Technology (ART) and non-ART fertility treatments (which are fertility drugs that induce or enhance ovulation in women and which can be used with timed intercourse or intrauterine insemination without the intention to perform ART. ART refers to fertility treatments in which eggs or embryos are handled in the laboratory with the purpose of establishing a pregnancy, such as in vitro fertilization with or without intracytoplasmic sperm injection (29). Non-ART fertility treatments may include medical therapies like ovulation-stimulating drugs and intrauterine insemination (IUI).

2.2.1. In-vitro fertilization and Intracytoplasmic sperm injection

In-vitro fertilization (IVF) is the most common ART technique, which involves the retrieval of eggs from the woman’s ovaries, which are then fertilized with sperm in a laboratory setting. IVF is often carried out alongside other procedures, such as intracytoplasmic sperm injection (ICSI), to increase the chances of success. According to a study in 2023 by N. Muhaydat and colleagues, 48.3% had successful IVF and embryo transfer (ET) that resulted in clinical pregnancy (30). A study conducted in Ethiopia in 2021 shows the clinical pregnancy rate of IVF to be 30.1% (31).

2.2.2. Intrauterine insemination and ovulation induction

Ovulation induction, usually combined with intrauterine insemination, is another common fertility treatment option. This method involves stimulating egg production in women's ovaries using medications and then introducing sperm into the uterus during the woman's fertile window. According to the Yale Fertility Center in America, intrauterine insemination has a 20 – 25 percent success rate of pregnancy per cycle (32). A retrospective analysis of IUI by Immediata et al. (2020) showed that the overall success rate of IUI per cycle is 10 – 20% (33). A study investigating the success of controlled ovarian hyperstimulation with intrauterine insemination in women who underwent surgical procedures to treat endometriosis, Controlled Ovarian Hyperstimulation (COH)+IUI did not improve pregnancy rates in any of the stages of endometriosis (34). Even though the success rate of IUI is lower than that of IVF, it can be a "worthy first step" for couples who are new and trying ART for the first time (33). Another advantage of IUI over IVF is that it is simple and relatively cheaper.

2.3. Factors affecting treatment outcome of infertility

2.3.1. Sociodemographic factors

2.3.1.1. Age

Age can be a major factor that influences the treatment success of infertility. The Yale Fertility Center identifies age as a factor that influences the success rate of IUI (32). A study conducted in Romania to assess the impact of a one-year age difference on the outcomes of IVF treatment for patients aged 34, 35, and 36 found that women aged 34 and 35 had higher clinical pregnancy rates compared to women aged 36 (35). Another study from China found that women who are below the age of 35 have a higher clinical pregnancy rate and live birth rate than the advanced age group, and that age is also a risk factor for miscarriage (36). A study in Namibia found that 64% of the women who had failed ART treatment were women who exceeded the age of 30 (37). On the other hand, a study conducted in Ethiopia states that fertility from fertility-inducing drugs tends to increase as age advances until the women reach 40 years, where it declines again. The age group 20-29 has a 27.7% rate of fertility, while the age group 30-39 has a 57.1% rate. This decreases to 14.1% of the pregnancy rate when age exceeds 40 years (38).

2.3.1.2. Residence

The place of residence can be a factor in influencing the treatment of infertility. Distance from fertility centers and lack of treatment in small centers have been reported to have an impact on treatment seeking behavior and treatment adherence in a study conducted in Iran (39).

2.3.2. Duration of infertility

There is evidence that the duration of infertility can impact the treatment outcome. In a study conducted in Iraq, it was found that males who suffered from infertility for less than four years had higher pregnancy and live birth rates compared to those who suffered for more than 10 years, which also suffer a higher abortion rate (40). There is also evidence that IUI requires the couple to have less duration of infertility to have good success compared to IVF (41).

2.3.3. Type, factor and etiology of infertility

The type of infertility can have a tendency to influence the treatment outcome of infertility (42). A study conducted in Poland suggested that isolated male factor infertility or combined male and female factor infertility have a negative impact on the treatment outcome (43). According to a Namibian study, with a success rate of 37.8%, secondary infertility is more successful than primary infertility, which has a success rate of 29.2% (37). Endometrial thickness is also associated with it. The pregnancy rate of women after IVF with an EMT below 7mm is significantly lower than that of women with an EMT above 7mm (44).

2.3.4. Underlying health conditions

There is evidence that underlying health conditions may affect the treatment outcome of infertility. Women with endocrine disorders are found to have significantly less success in their IVF outcome even after proper treatment (45). Autoimmune diseases are the other factors that affect the treatment success of ART. For instance, Antinuclear antibody (ANA) positivity is associated with lower clinical pregnancy rate (CPR) and higher miscarriage rate (46).

2.3.5. Lifestyle

Lifestyle, such as smoking and alcohol consumption tend to have an impact on the treatment outcome. According to a study conducted in Western Australia, smoking tends to decrease ovarian reserve and increase pregnancy loss. But male alcohol consumption was found to have a

positive effect on fertilization (47). This relationship appears to not be well understood. However, the authors speculated that consuming fruits and vegetables increased the rates of fertilization according to that study, and there appears to be a significant interaction between alcohol consumption and intake of fruits and vegetables.

2.3.6. Number of treatment cycles

Women receiving ART treatment for the first time had a success rate of 31.5%; those receiving treatment for two cycles had the highest success rate (42.1%), but women who had more than two cycles of ART treatment were found to have the lowest success rate (20%) (37). This indicates that the number of cycles of treatment can determine the treatment outcome of infertility on top of other factors.

In summary, infertility remains a neglected public health issue despite its high prevalence worldwide. While fertility treatment centers are emerging in Ethiopia, there is a notable scarcity of studies investigating success rates, factors influencing success, and the time to live birth. Various factors may adversely affect the outcome of infertility treatments, including the duration of infertility and underlying health conditions, with increased duration or the presence of certain health issues negatively affecting its success rate. The impact of women's age on treatment success has generated conflicting findings in the reviewed literatures. Moreover, the etiology of infertility, lifestyle choices such as smoking and alcohol consumption, and the number of treatment cycles are additional elements that can influence the success of infertility treatments. Further research in these areas is imperative for a comprehensive understanding and effective management of infertility in the Ethiopian context.

2.4. Conceptual framework

The conceptual framework is developed after reviewing various literatures. Specific infertility factors, such as male or female factors, contribute to the selection of a particular type of treatment. For example, IUI is considered first-line for male factor infertility (48). Underlying health conditions may negatively affect the treatment outcome. For instance, endocrine disorders negatively influence ovarian function, which in turn affects the pregnancy rate (45). The chosen infertility treatment modality directly influences the ultimate outcome, whether it is success or failure. IUI has a relatively lower success rate than IVF (33). The outcome of the treatment may

influence the decision to undergo additional treatment cycles, and the number of cycles in turn may affect the ultimate outcome. The duration of infertility has an impact on the likelihood of treatment success or failure (40). Both the type of infertility and lifestyle choices, such as smoking and alcohol use, can influence the ultimate success or failure of infertility treatment (37,47).

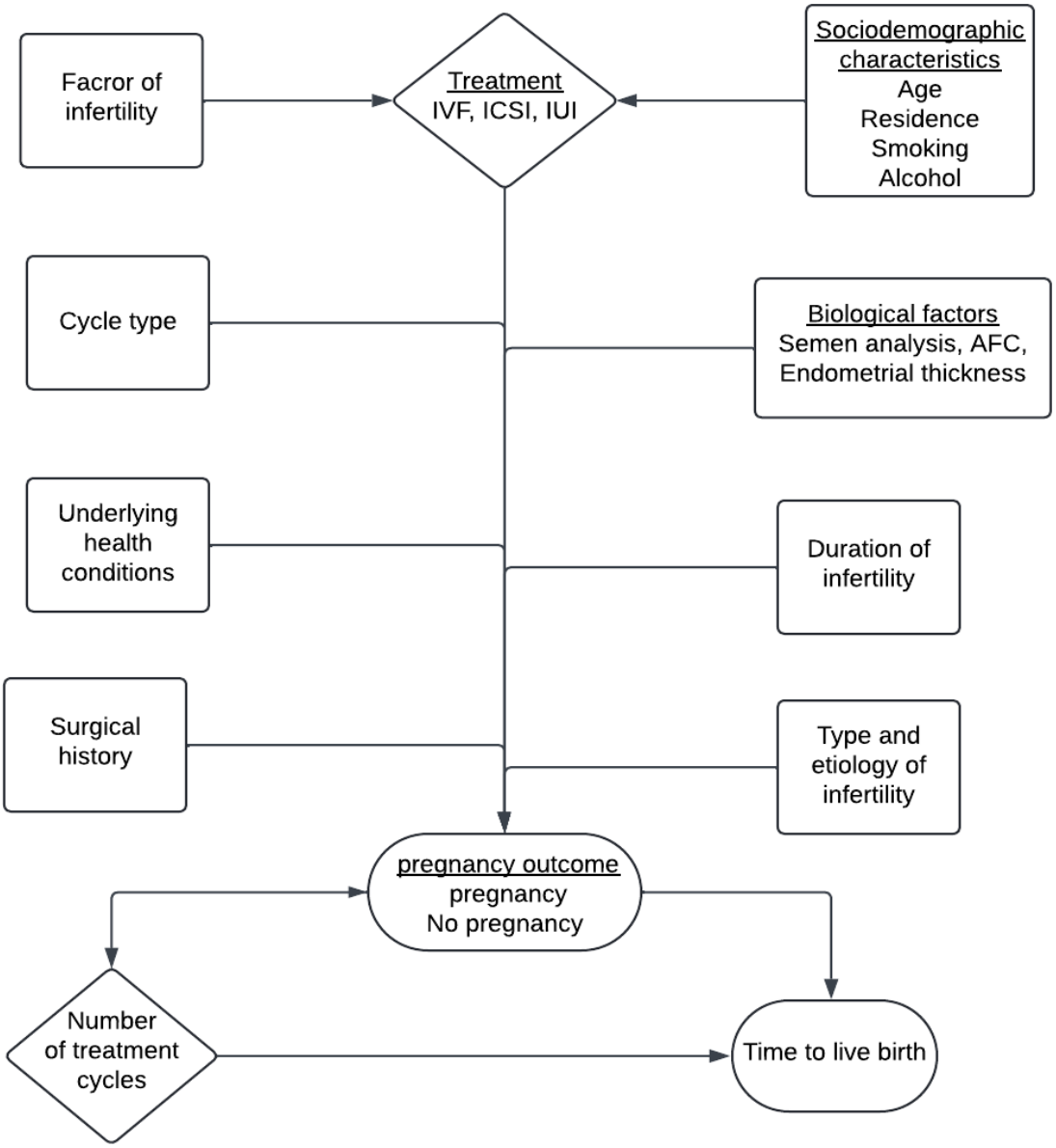

Figure 1. Conceptual framework for factors associated with fertility treatment success among couples attending fertility centers in Addis Ababa, Ethiopia, 2021-2023.

3. Objectives

3.1. General objective

To assess the treatment success rate and time to live birth of fertility treatments among couples attending public and private fertility centers in Addis Ababa, Ethiopia, 2023

3.2. Specific objectives

1. To determine the treatment success rate of infertility among couples who have undergone fertility treatments.
2. To identify factors influencing treatment success rate among couples who have undergone fertility treatments.
3. To calculate time to live-birth of fertility treatments among couples who have undergone fertility treatments.
4. To identify factors associated with time to live-birth of fertility treatments among couples who have undergone fertility treatments.

4. Methods

4.1. Study setting

According to information obtained from the Ethiopian Federal Ministry of Health, there are four licensed and functional fertility centers in Ethiopia, all located in Addis Ababa. Of the four centers, one is a public fertility center, and the other three are private centers. From the three private fertility centers, only one was willing to collaborate and provide data for this study. Therefore, this study was conducted at that particular private center in addition to the only public fertility center in Ethiopia.

The first fertility center is Michu Clinic; Center for Fertility and Reproductive Medicine, which is a public fertility center under Saint Paul's Hospital Millennium Medical College's (SPHMMC) department of obstetrics and gynecology and is located in Addis Ababa, the capital city of Ethiopia. SPHMMC operates as a Federal Ministry of Health (FMOH) tertiary teaching referral hospital. The center for fertility and reproductive medicine is Ethiopia's first public IVF center since it opened its doors to patients in February 2019 (49). The second fertility center included in this study is Ethio fertility and IVF Center, which is a private fertility center that was opened to service in 2021. The center provides male and female infertility treatment, including assisted reproductive technology, namely IVF, ICSI, and IUI; minimally invasive surgeries like laparoscopy and hysteroscopy; and OBGYN consultations.

4.2. Study design

An institution-based retrospective record review was conducted at SPHMMC and Ethio Fertility and IVF in Addis Ababa City from March 2021 to February 2023. This time frame was selected so that the last treatment initiation date will be more than 10 months prior to our data collection time. This will ensure that we fully observe the pregnancy outcomes until birth. A two-year retrospective data extraction from clients' charts was conducted and follow up time was 36 months to exclusively observe every possible outcome of the pregnancy including live birth.

4.3. Source and study population

4.3.1. Source population

All married or cohabiting infertile couples who have undergone fertility treatments in Addis Ababa.

4.3.2. Study population

Infertile couples who have undergone fertility treatment at SPHMMC and Ethio fertility and IVF center in Addis Ababa from 2021-2023.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

- Couples who have undergone IVF/ICSI and IUI fertility treatments from March 2021 to February 2023.

4.4.2. Exclusion criteria

- All infertile couple who left their treatment cycle incomplete

4.5. Sample size determination

Sample size determination for objective 1:

The expected proportion of success for IVF is 30.1%, according to a previous cross-sectional study in Addis Ababa (31). Assumptions considered are a 95% confidence level and 80% power. The sample size was calculated using the Cochran formula as follows:

$$n = \frac{(Z\alpha/_2{}^2)\times P(1-P)}{d^2} \text{----------(1)}$$

Calculating this, we get a value of 323. Accounting for a 10% non-response rate, the final required sample size becomes **356**.

Sample size determination for objective 2:

Among factors affecting treatment success, the second treatment cycle has the highest value, with a proportion of success of 42.1%, according to a Namibian study (37). The sample size calculation formula is as follows:

$$n = \frac{(Z\alpha/_2{}^2)\times P(1-P)}{d^2} \text{ ----------(2)}$$

After calculation, the sample size becomes 375. Accounting for the 10% non-response rate, the final sample size becomes **414**.

Sample size determination for objective 3:

We calculated the minimum required sample size using the survival analysis sample size calculation using the hazard ratio and median survival time. These two components were taken from a previous cohort study in Australia (2018) (50) due to the lack of previous studies in Ethiopia.

Assumptions considered are a 95% confidence interval and 80% power. The sample size was calculated using the log-rank test using the following formula:

$$n = \frac{4\times(Z_{\frac{\alpha}{2}} + Z_{1-\beta})^2 \times (\frac{1}{HR})^2 \times (MST)^2}{\pi^2} \text{ ----------(3)}$$

Where,

n= the required sample size

Zα/2= 1.96 (the critical value at $\frac{\alpha}{2}$ for a two-tailed test from the standard normal distribution)

*Z*1−*β*= 0.84 (the critical value at 1−*β)*

HR (hazard ratio) = 0.96

MST (median survival time) = 8.9 months

The final number of samples calculated was 273 couples. To account for censoring, the sample size is adjusted as follows.

$$n_{adjusted} = \frac{n}{1 - estimated\ proportion\ of\ event}$$

The estimated proportion of success (clinical pregnancy rate) of IVF in Addis Ababa in 2020 was 30.1% (31). After adjusting, the final total sample size will be **390**.

The largest sample size is **414** samples, and we used that as the final sample size.

4.6. Sampling techniques and procedures

In order to obtain a representative sample from our list of patients, we employed a simple random sampling technique using the serial numbers assigned to each patient. The list of patients with their respective chart registration numbers is available in the centers' databases. We used the serial number of the list of patients starting from March 1, 2021, to February 29, 2023, to randomly draw a total of 414 samples targeted for inclusion, with the use of a random number generator to select patient serial numbers without bias or predictability. This process ensures that each patient on the list has an equal chance of being chosen, contributing to the overall representativeness of the sample. The sampling was from couples who have already completed at least one IVF/ICSI or IUI treatment cycle, and those who have not were already excluded before the sampling procedure takes place. We proportionally allocated the samples to both facilities according to the proportion of treated patients over the two-year period.

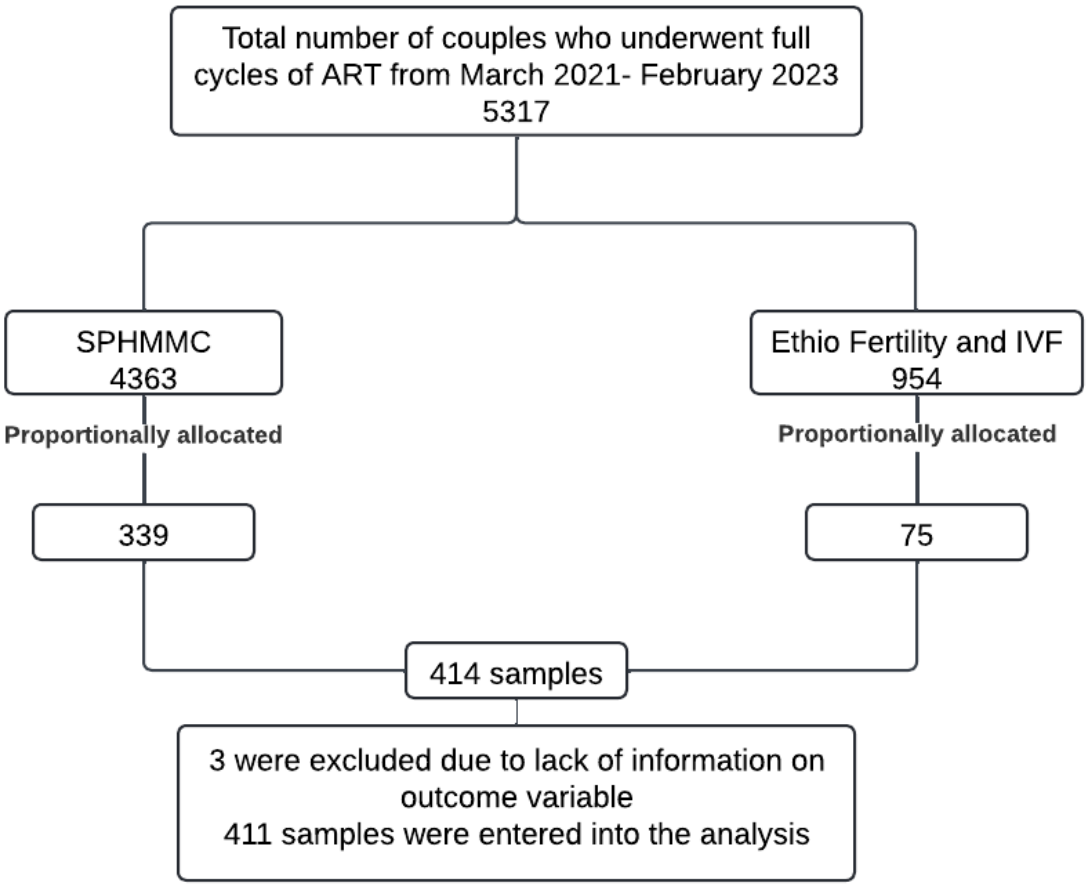

Figure 2. General description of allocation of samples to both fertility centers

4.7. Data collection procedures

Data collection was conducted through the use of a data abstraction format and a questionnaire by the use of Kobo toolbox. A review of the demographic and medical data of the selected couple was extracted from the patients' charts using the data abstraction format. The data abstraction format captures information related to socio-demographic characteristics, infertility treatment details, clinical and laboratory data, and treatment outcomes in terms of clinical pregnancy. It is organized into four parts: socio-demographic characteristics, infertility treatment information, clinical and laboratory data, and outcome and follow-up.

After collecting data from the medical chart, those with successful clinical pregnancies was contacted, and a questionnaire was administered using a phone call for information regarding pregnancy outcomes. The questionnaire was developed in English, translated into Amharic to enhance participants' understanding, and then back-translated to English for consistent and accurate data analysis. It focused on gathering information related to pregnancy outcomes resulting from infertility treatments. The information sheet was read to the participants over the phone, and oral informed consent was obtained. Only then they were asked to provide information regarding their pregnancy outcomes. Data from both patient medical chart and phone interview was collected by trained health professionals who already work in the two treatment centers. It was collected from March 1 to March 31, 2024.

The data abstraction format and questionnaire were adopted after reviewing various literatures (12,31,38,51). Pretest was conducted on 5% of the sample in the study setup (SPHMMC) to ensure quality and was modified accordingly. The data was collected after the employment and training of three data collectors with bachelor's degrees in nursing and one supervisor who is a candidate for Master of public health degree. They were selected for their relevant educational backgrounds, clinical and research experience, adherence to ethical standards, strong communication skills, and ability to ensure high-quality data collection.

4.8. Study variable

4.8.1. Dependent variable

- The outcome of fertility treatments (clinical pregnancy)
- The time to live birth

4.8.2. Independent variable

- Sociodemographic characteristics (Age, residence, smoking and alcohol)
- Underlying health conditions (diabetes mellitus, hypertension, autoimmune diseases, HIV/AIDS, cardiac problems, thyroid problems and TB)
- surgical history
- duration of infertility

- factor of infertility (male factor, female factor, combined factor unexplained infertility)
- Type of infertility (primary infertility and secondary infertility)
- Etiologies of infertility
- Biological factors (semen analysis, endometrial thickness and AFC)
- Type of treatment
- Number of treatment cycles
- Cycle type

4.9. Operational definition

- **Primary infertility**- when a pregnancy has never been achieved by a person (5)
- **Secondary infertility**- at least one prior pregnancy has been achieved (5)
- **Clinical pregnancy**- presence of gestational sac and heart beat detected by ultrasonography 4 weeks after embryo transfer or insemination (52).
- **Treatment success**- clinical pregnancy rates per started cycle, oocyte retrieval or embryo transfer (53).
- **Complete cycle**- All embryo transfer attempts (fresh and frozen) resulting from one episode of ovarian stimulation(54)
- **Live birth**- complete expulsion or extraction of a product of human conception, irrespective of the duration of pregnancy, that, after such expulsion or extraction, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached (55). This usually occurs between 37-42 weeks of gestation.
- **Miscarriage** - a spontaneous loss of a previable pregnancy which is a fetus weighing less than 500g or gestational age of below 20 weeks (56).
- **Endometrial thickness**- is the measurement of the lining of the uterus or the endometrium.
    - $\leq$7mm- thin
    - $8-14$- Optimal

- >14- thick (44)

- **Antral Follicle Count** – measure of the number of follicles on the ovaries, using an ultrasound examination. The AFC provides insights into a woman's ovarian reserve and potential fertility status.
  - ≥5 – Normal
  - <5 – Abnormal(low) (31)

4.10. Data management

All data collected including participant information was treated with strict confidentiality. Data was collected by data collection software using secure electronic devices, and access was restricted to authorized personnel only. Regular backups were implemented to prevent data loss. Data quality checks were conducted during and after the data collection process to identify and rectify any errors promptly.

4.11. Data analysis procedures

After data collection, the data was checked for completeness, cleaned, and coded, which was then exported to SPSS (statistical package for social science) version 26 and STATA statistical software version 17 for further management and analysis. For categorical data, descriptive statistics like frequency and percentages were computed and presented through the use of tables, graphs, and pie charts. Continuous variables were summarized by using means, medians, and standard deviations after checking the distribution.

For the first and second objectives, descriptive and binary logistic regression were used to analyze the association between treatment outcome and potential predictor variables. For the third and fourth objectives, survival methodologies were utilized to analyze the time to success for infertility treatment. We used the Kaplan-Meier, Life-Table and Log-rank test to analyze the survival probabilities of success over time. Additionally, we used Cox regression analysis to identify factors that significantly influence the time to Live birth in infertility treatments after all necessary assumptions were checked.

Bivariate analysis was conducted, and variables with p-value <0.25 were entered into multivariable analysis in both logistic regression and survival analysis methods. A variable with a p-value <0.05 was interpreted as having a statistically significant association with the outcome variables in the multivariable analysis. Adjusted odds ratios and adjusted hazard ratios were used

to report the relationship between outcomes and predictor variables. Tables, graphs and Texts were used to describe and visualize the results.

4.12. Data quality assurance

The data abstraction format is prepared in English. The questionnaire used for phone interview was first prepared in English and translated into Amharic for better understanding of the respondents. A two-days training was provided for the data collectors and the supervisor on how to better understand the tools, the data collection method, and how to approach the respondents. Pretest was conducted on 5% of the samples before starting the data collection, and some modifications were made. There was close supervision of data collectors, and data was checked for completeness on a daily basis.

4.13. Ethical consideration

Ethical clearance was obtained from the Research Ethics Committee of the School of Public Health at Addis Ababa University and St. Paul's hospital millennium medical college. A waiver of informed consent was obtained from the health facilities regarding the data abstraction from patients' charts because of feasibility issues in obtaining informed consent. For the questionnaire, informed oral consent was obtained from participants, clearly explaining the purpose, procedures, potential risks, and benefits of the study. Confidentiality, anonymity, and data security were ensured. Voluntary participation was followed by allowing participants to withdraw from the study at any time without consequences.

4.14. Dissemination of findings

The results of this study will be submitted to Addis Ababa University, School of Public Health, and a final thesis defense will be conducted. We aim to publish our findings in reputable peer-reviewed journals in the field of public health or reproductive health. We will present our findings at relevant conferences and seminars to reach a wider audience of professionals in the field.

5. Results

5.1. Sociodemographic characteristics of patients with infertility in terms of clinical pregnancy

A total of 411 samples of patients were entered into the analysis of this study after excluding 3 samples for missing information on their status of clinical pregnancy (outcome variable). A medical chart review was made for all of the participants and a phone interview was conducted for 192 of couples with positive clinical pregnancy over the phone.

More than half of the women who underwent fertility treatments were younger than 35 years of age 211(51.3%), while a slightly smaller cohort falls within the age category of 35 and above (48.7%). The mean age of the women is 35 (SD ±5). Looking at the geographical distribution of our sample, we found that 266 (64.7%) participants reside in Addis Ababa, while 145 (35.3%) couples live outside the city. In regards to lifestyle factors, it was revealed that there are varied patterns of behavior among the participants. While the majority of the samples (93.2%) reported abstaining from smoking and alcohol consumption, there was a notable proportion of reports regarding alcohol use (4.1%). In relation to treatment facility, there appears to be relatively balanced clinical pregnancy and no statistically significant difference was observed between the two facilities (Table 1).

Table 1. Sociodemographic characteristics of women undergoing fertility treatments in Addis Ababa, Ethiopia, 2021-2023.

Variable	**Category**	**Outcome**	
		No pregnancy n (%)	**Pregnancy n(%)**
Age of the women	<35	66(31.3)	145(68.7)
	≥35	153(76.5)	47(23.5)
Residence	Addis Ababa	137(51.5)	129(48.5)
	Out of Addis Ababa	82(56.6)	63(43.4)
Smoking	No	213(53.3)	187(46.7)
	Yes	6(54.5)	5(45.5)
Alcohol	No	213(54.1)	181(45.9)
	Yes	6(35.3)	11(64.7)
Treatment facility	Ethio fertility and IVF	45(60.8)	29(39.2)
	SPHMMC	174(51.6)	163(48.4)

5.2. Clinical characteristics of women with infertility in terms of clinical pregnancy

Of the total 411 participants, the medical chart of the couple reports only 57 (13.8%) women having underlying health conditions. Among those with underlying health conditions, Diabetes Mellitus (DM) was reported by 13 women (22.8%), while Hypertension (HTN) was prevalent in 23 couples (40.4%). A smaller proportion of individuals report cardiac problems (1.8%), HIV (12.3%), autoimmune conditions (3.5%), thyroid issues (14%), and Tuberculosis (TB) (14%). No individual reported kidney disease or other endocrine disorders among this subset of the population.

Furthermore, a total of 75 women (18.2%) reported a history of previous surgical procedures, while the majority (81.8%) did not. Among those with surgical history, pelvic or abdominal surgeries were the most common, reported by 56 women (74.7%). Ovarian or fallopian tube surgeries were reported by 20 women (26.7%), while a smaller proportion report other surgery, specifically hemorrhoidectomy (2.7%) (Table 2).

Table 2. Clinical characteristics of women undergone fertility treatments in Addis Ababa, Ethiopia, 2021-2023

Variables	**Categories**	**Outcome**	
		No pregnancy n(%)	**Pregnancy** n(%)
Underlying health conditions	No	177(50%)	177(50%)
	Yes	42(73.7%)	15(26.3%)
DM	No	206(51.8)	192(48.2)
	Yes	13(100)	0(0)
HTN	No	201(51.8)	187(48.2)
	Yes	18(78.3)	5(21.7)
Cardiac problems	No	218(53.2)	192(46.8)
	Yes	1(100)	0(0)
HIV/AIDS	No	213(52.7)	191(47.3)
	Yes	6(85.7)	1(14.3)
Autoimmune	No	217(53.1)	192(46.9)
	Yes	2(100)	0(0)
Thyroid problems	No	215(53.3)	188(46.7)
	Yes	4(50)	4(50)
TB	No	216(53.6)	187(46.4)
	Yes	3(37.5)	5(62.5)
Surgical history	No	170(50.6%)	166(49.4%)
	Yes	49(65.3%)	26(34.7%)
Pelvic/Abdominal surgery	No	178(50.1)	177(49.9)
	Yes	41(73.2)	15(26.8)
Ovarian/Fallopian tube surgery	No	210(53.7)	181(46.3)
	Yes	9(45)	11(55)
Other surgery	No	217(53.1)	192(46.9)
	Yes	2(100)	0(0)

Footnote: DM; Diabetes Mellitus, **HTN**; Hypertension, **TB**; Tuberculosis

5.3. Infertility profile in terms of clinical pregnancy

Of the couples who underwent fertility treatments, those with primary infertility constitute the majority (56.9%), while those with secondary infertility makeup 43.1% of the couples (Figure 3). This analysis reveals a notable prevalence of female factor infertility, accounting for 48.4% of cases. Concurrently, male factor infertility was identified in 18%, combined factor in 3.6%, and a significant proportion of unexplained infertility (29.9%) was identified. The mean duration of infertility among the couples is 6.73(SD±3.87) years.

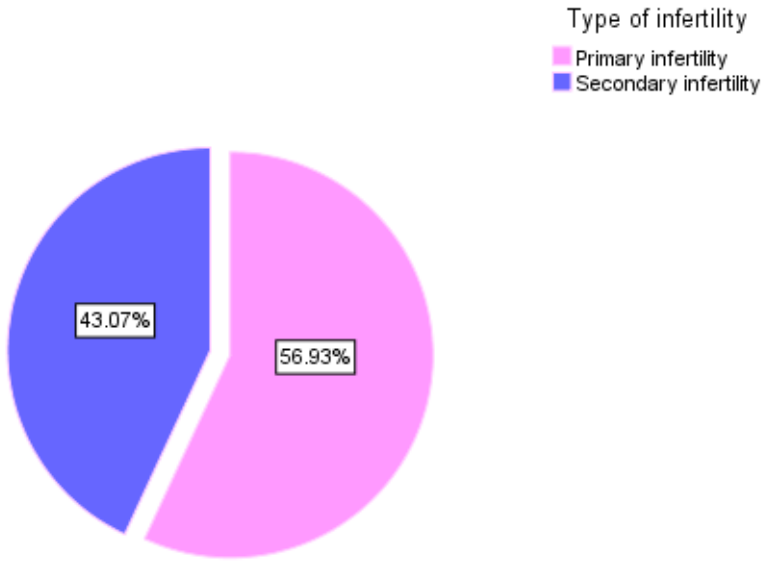

Figure 3. Type of infertility of couples who undergone fertility treatment in Addis Ababa, Ethiopia, 2021-2023.

5.4. Biological factors in terms of clinical pregnancy

More than three fourth 315 (76.6%) of the women present with AFC greater than 5. However, the rest 23.4% exhibit AFC counts below 5, which is low or considered abnormal. Similarly, the result of semen analysis among male participants demonstrates 77.6% normal semen parameters. Twenty two percent of male participants exhibit low semen analysis results, which may include abnormalities in sperm concentration, motility, or semen volume. 282(68.6%) of the women had optimal endometrial thickness. Seventy-one (17.3%) had thin endometrium, and 58(14.1%) had thick endometrium at the day of ovulation triggering (Table 4).

Table 3. Clinical characteristics of women undergone fertility treatments in Addis Ababa, Ethiopia, 2021-2023

Variables	**Categories**	**Outcome**	
		No pregnancy N(%)	**Pregnancy N(%)**
AFC	≥ 5	140(44.4)	175(55.6)
	<5	79(82.3)	17(17.7)
Semen analysis	Normal	168(52.7)	151(47.3)
	Abnormal	51(55.4)	41(44.6)
Endometrial thickness	Optimal	107(38.2)	175(62.5)
	Thin	59(83.1)	12(16.9)
	Thick	53(91.4)	5(8.6)

Footnote; **AFC;** Antral follicle count

5.5. Fertility treatment methods and characteristics in terms of clinical pregnancy

From the total 411 couples, 222(54%) used conventional IVF (cIVF). A total of 250 cycles of cIVF were performed in our samples. From those who had cIVF, 197(88.7%) had only 1 cycle of cIVF, 22(9.9%) underwent 2 cycles, and 3(1.4%) underwent 3 cycles. Intracytoplasmic sperm injection (ICSI) was performed on 134(32.6%) of the couple and 147 cycles in total. There was only a maximum of 2 cycles of ICSI in which the majority 122(91%) of them underwent 1 cycle and the rest 12(9%) underwent 2 cycles. More than one third 164(39.9%) of the couples had IUI, of which nearly half 79(48.2%) of them had only 1 cycle of IUI procedure, while similar proportion of them had 2 and 3 cycles making the total performed cycles of IUI 299 as shown in Table 4.

Table 4. Description of fertility treatment methods and characteristics of couples who underwent fertility treatments in Addis Ababa, Ethiopia, 2021-2023

Variables	**Categories**	**Outcome**	
		No pregnancy n(%)	**Pregnancy n(%)**
IVF	No	123(65.1)	66(34.9)
	Yes	96(43.2)	126(56.8)
Number of IVF cycle	1 cycle	92(46.7)	105(53.3)
	2 cycles	3(13.6)	19(86.4)
	3 cycles	1(33.3)	2(66.7)
ICSI	No	152(54.9)	125(45.1)
	Yes	67(50)	67(50)
Number of ICSI cycle	1 cycle	66(54.1)	56(45.9)
	2 cycles	1(8.3)	11(91.7)
IUI	No	116(47)	131(53)
	Yes	103(62.8)	61(37.2)
Number of IUI cycle	1 cycle	61(77.2)	18(22.8)
	2 cycles	26(66.7)	13(33.3)
	>2 cycles	16(34.8)	30(65.2)
Cycle type	Fresh	91(46.7)	104(53.3)
	Frozen	128(59.3)	88(40.7)
Total number of treatment cycle		Mean 1.69 (SD±0.9)	

5.6. Fertility treatment outcome in terms of clinical pregnancy

Out of the total 411 couples who underwent Assisted reproductive technology, 192(47%) were able to achieve successful clinical pregnancy. Out of these successes, 98(51%) were from IVF, 58(30.2%) were from ICSI and 36(18.8%) were from IUI.

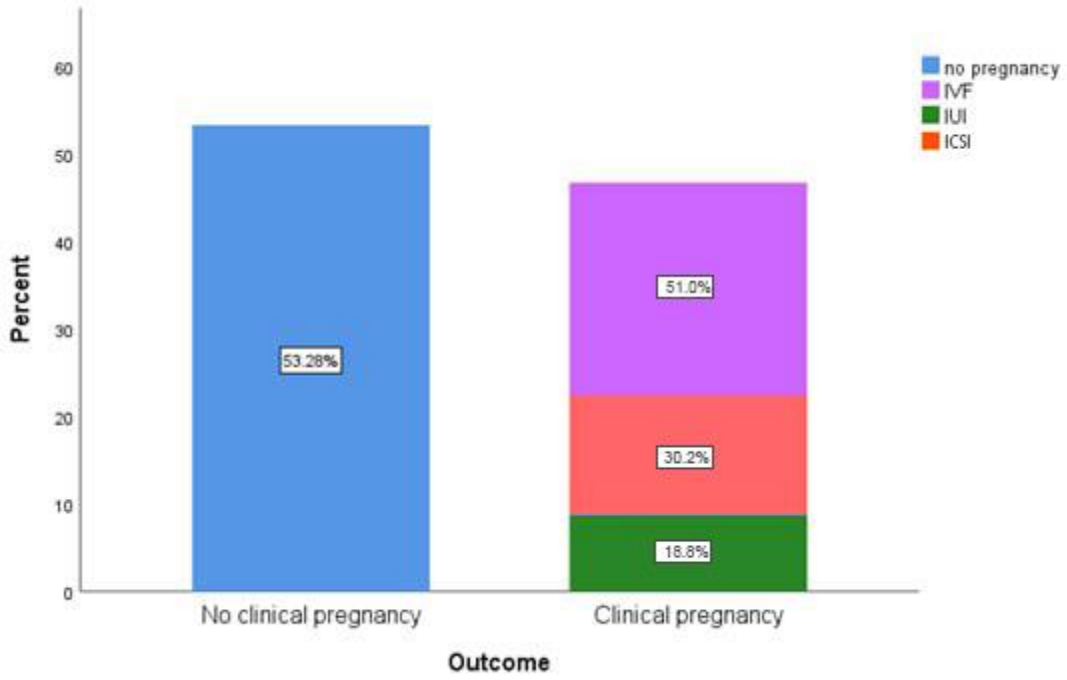

Figure 4. Clinical pregnancy outcome and proportion of treatment methods of couple who underwent assisted reproductive technology in in Addis Ababa, Ethiopia, 2021-2023

The cumulative clinical pregnancy rate of IVF/ICSI after a maximum of 3 cycles is 70.6%. Separating by fertilization protocol, ICSI has a cumulative clinical pregnancy rate of 43.3% with a maximum of 2 cycles, and conventional IVF has 44.1% clinical pregnancy rate with a maximum of 3 cycles. IUI has 21.9% after a maximum of 4 cycles. However, when we take into account the number of treatment cycles, the clinical pregnancy rate of IVF is 39.2% per cycle. ICSI has 39.4% and IUI has 12% clinical pregnancy rates per cycle.

5.7. Factors associated with treatment success (Clinical pregnancy)

The association of the predictor variables with the outcome of clinical pregnancy of the assisted reproductive technology was investigated by the use of both bivariate and multivariable logistic regression analysis. According to the bivariate analysis, age, underlying health conditions, DM,

HTN, HIV, female factor infertility, combined factor infertility, tubal factor, sexual dysfunction, duration of infertility, AFC count, endometrial thickness, fresh IVF cycle, frozen IVF cycle, and total number of cycles showed association with clinical pregnancy rate of assisted reproductive technology (P-value < 0.25). For this reason, they were used in the multivariable analysis.

In the multivariable analysis, women's age appears to be significantly associated with the success of ART. Women whose age was below 35 years had 4 times (AOR= 4.016; 95% CI: 2.292, 7.036) higher odds of successful clinical pregnancies compared to the women aged 35 years and above. From different types of etiologies of infertility, Tubal factor infertility and sexual dysfunction showed significant association with the success of the treatment. Tubal factor infertility showed a negative relationship with the success of the treatment in that couples, where the women had tubal factor infertility, had 58% lower odds (AOR= 0.419; 95% CI: 0.188, 0.936) of achieving clinical pregnancy compared to those without tubal factor infertility, while controlling for other factors. Couples with sexual dysfunction had over six times higher odds (AOR= 6.270; 95% CI: 1.235, 31.842) of having successful ART treatments compared to those without. The duration of infertility had a significant negative association with treatment outcomes. For each additional year of infertility, there was a 15% decrease in the odds of successful ART treatment (AOR= 0.851; 95% CI: 0.784, 0.922).

Women with an AFC count of 5 and above had 2.2 times higher odds (AOR= 2.228; 95% CI: 1.074, 4.624) of achieving success compared to those whose follicular count was below 5. Endometrial thickness was another factor significantly associated with the treatment outcome of ART. Women with a thin endometrium on the day of ovulation triggering had 76.3% lower odds (AOR= 0.237; 95% CI: 0.097, 0.578) of achieving successful clinical pregnancies, and women with a thick endometrium had 95% lower odds (AOR= 0.05; 95% CI: 0.016, 0.154) of success compared to women with optimal endometrial thickness.

The total number of treatment cycles showed a significant association with the outcome. For each additional cycle, there were 1.8 times higher odds of success (AOR= 1.826; 95% CI: 1.353, 2.464). The total number of frozen cycles also had a significant positive association with the success of ART, where each additional frozen cycle undertaken increased the odds of success by 3.5 times (AOR= 3.459; 95% CI: 1.967, 6.085).

Table 5. Factors associated with success of ART treatment among couples underwent fertility treatments in Addis Ababa, Ethiopia, 2021-2023

Variables	Categories	Outcome		COR (95% CI)	AOR (95% CI)	P-value
		No pregnancy (%)	Pregnancy (%)			
Age	<35	66(30.1)	145(75.5)	7.15(4.62-11.08)	4.02(2.29-7.04)	**<0.001***
	≥35	153(69.9)	47(24.5)	**Ref**	**Ref**	
Underlying health conditions	No	177(80.8)	177(92.2)	**Ref**	**Ref**	
	Yes	42(19.2)	15(7.8)	0.357(.191-.667)	1.003(0.339-2.970)	0.995
HTN	No	201(91.8)	187(97.4)	**Ref**	**Ref**	
	Yes	18(8.2)	5(2.6)	0.299(0.109-0.820)	0.538(0.104-2.793)	0.461
HIV	No	213(98.6)	191(99.5)	**Ref**	**Ref**	
	Yes	6(2.7)	1(0.5)	0.186(0.022-1.558)	0.503(0.014-17.47)	0.704
Surgical history	No	170(50.6)	166(49.4)	**Ref**	**Ref**	
	Yes	49(65.3)	26(34.7)	0.543(0.323-0.915)	0.911(0.427-1.941)	0.808
Female factor infertility	No	106(48.4)	106(55.2)	**Ref**	**Ref**	
	Yes	113(51.6)	86(44.8)	0.761(0.516-1.123)	1.622(0.737-3.57)	0.229
Combined factor infertility	No	214(97.7)	182(94.8)	**Ref**	**Ref**	
	Yes	5(2.3)	10(5.2)	2.35(0.789-7.005)	3.26(0.69-15.37)	0.135
Tubal factor infertility	No	131(59.8)	135(70.3)	**Ref**	**Ref**	
	Yes	88(40.2)	57(29.7)	0.629(0.417-.948)	0.419(0.188-0.936)	**0.034***
AFC count	<5	79(36.1)	17(8.9)	**Ref**	**Ref**	
	≥5	140(63.9)	175(91.1)	5.809(3.288-10.26)	2.228 (1.074-4.624)	**0.031***
Endometrial thickness	Optimal	107(48.9)	175(91.1)	**Ref**	**Ref**	
	Thin	59(26.9)	12(6.3)	0.124(0.064-.242)	0.237(1.074-4.624)	**0.001***
	Thick	53(24.2)	5(2.6)	0.058(0.022-.149)	0.05(0.016-0.154)	**<0.001***
Duration of infertility	Mean= 6.73 (SD±3.7)			0.785(0.735-.838)	0.851(0.784-0.922)	**<0.001***
Total number of frozen cycles	Mean= 0.34 (SD±0.63)			3.462(2.295-5.224)	3.459(1.967-6.085)	**<0.001***
Total number of cycles	Mean=1.69(SD±0.9)			1.654(1.309-2.088)	1.826(1.32-2.525)	**<0.001***

Footnote: **Ref:** Reference category; **HTN**: Hypertension; **TB**: Tuberculosis; **AFC**: Antral follicle count

To assess the adequacy of the logistic regression model, the Hosmer-Lemeshow goodness-of-fit test was conducted. The chi-square statistics for the Hosmer-Lemeshow test was calculated to be 5.089 (df=8, p=0.748). The non-significant p-value (>0.05) indicates that the regression model adequately fits the data at 95% CI.

5.8. Sociodemographic characteristics of patients with infertility in terms of live birth

The majority of the women were below 35 years old. There appears to be a higher experience of live birth among women aged below 35 years compared to women aged 35 and above with a significant chi-square test (x^2=38.931, p=<0.001). Place of residence, Life style, and Treatment facility appears to have no significant difference within their groups in terms of live birth outcome.

Table 6. Sociodemographic characteristics of women undergoing fertility treatments in terms of live birth in Addis Ababa, Ethiopia, 2021-2023.

Variable	**Category**	**Outcome**	
		No live birth n(%)	**Live birth n(%)**
Age	<35	112(53.1)	99(46.9)
	≥35	164(82)	36(18)
Residence	Addis Ababa	180(67.7)	86(32.3)
	Out of Addis Ababa	96(66.2)	49(33.8)
Smoking	No	268(67)	132(33)
	Yes	8(72.7)	3(27.3)
Alcohol use	No	266(67.5)	128(32.5)
	Yes	10(58.8)	7(41.2)
Treatment facility	Ethio fertility and IVF	54(73)	20(27)
	SPHMMC	222(65.9)	115(34.1)

5.9. Clinical characteristics of women with infertility in terms of live birth

Participants without underlying health conditions had a lower percentage of live births (35.3%) compared to those with such conditions (17.5%). The chi-square test revealed a significant association between the presence of underlying health conditions and live birth outcome (x^2= 7.026, df = 1, p = 0.008). Among participants with specific health conditions all participants with DM experienced no live birth, although this association was marginally significant ($\boldsymbol{x^2}$= 19.344, df = 1, p=0.055). Other conditions such as Hypertension (HTN), HIV, and Thyroid issues exhibited varying proportions of live births. Participants with a surgical history had a lower percentage of live births (22.7%) compared to those without (35.1%). The chi-square test indicated a significant association between surgical history and live birth outcome ($\boldsymbol{x^2}$= 4.31, df

= 1, p = 0.038). Among participants with previous surgeries Pelvic or abdominal surgeries were more prevalent among those who experienced no live birth (80.4%).

Table 7. Clinical characteristics of women undergoing fertility treatments in terms of live birth in Addis Ababa, Ethiopia, 2021-2023.

Variables	**Categories**	**Outcome**	
		No live birth n(%)	**Live birth n(%)**
Underlying health conditions	No	229(64.7)	125(35.3)
	Yes	47(82.5)	10(17.5)
DM	No	263(66.1)	135(33.9)
	Yes	13(100)	0(0)
HTN	No	255(99.2)	2(0.8)
	Yes	21(91.3)	2(8.7)
Cardiac	No	275(67.1)	135(32.9)
	Yes	1(100)	0(0)
HIV	No	270(66.8)	134(33.2)
	Yes	6(85.7)	1(14.3)
Autoimmune	No	274(67.0)	135(33.0)
	Yes	2(100)	0(0)
Thyroid problems	No	270(66.9)	133(33.1)
	Yes	6(75)	2(25)
TB	No	273(67.7)	130(32.3)
	Yes	3(37.5)	5(62.5)
Surgical history	No	218(64.9)	118(35.1)
	Yes	58(77.3)	17(22.7)
Pelvic/Abdominal surgery	No	231(65.1)	124(34.9)
	Yes	45(80.4)	11(19.6)
Ovarian/Fallopian tube surgery	No	262(67)	129(33)
	Yes	14(70)	6(30)
Other surgery	No	274(67)	135(33)

	Yes	2(100)	0(0)

5.10. Infertility profile and biological factors in terms of live birth

When considering the type of infertility, it was observed that among couples experiencing primary infertility, 65.0% did not achieve a live birth, while 35.0% did. On the other hand, for couples with secondary infertility, the percentage of those who did not achieve a live birth was slightly higher at 70.1%, with 29.9% successfully having a live birth. Among couples where the female partner was identified as the main factor, 69.3% did not have a live birth, while 30.7% did. In cases where the male partner was the primary factor, the percentage of couples without a live birth was slightly lower at 60.8%, with 39.2% achieving a live birth. For cases classified as unexplained infertility, 69.9% did not result in a live birth, and 30.1% did. Notably, among cases where a combined factor was identified, 46.7% did not have a live birth, while 53.3% did. Couples experiencing infertility for one year had an equal split, with 49.7% not achieving a live birth and 50.3% successfully having one. However, as the duration increased, the likelihood of achieving a live birth decreased. For instance, among couples dealing with infertility for three years, only 12.3% achieved a live birth, and for those with four years of infertility, the percentage was slightly higher at 24.0%. The mean duration of infertility for the couples in the study was found to be 6.73 years, with a standard deviation of ±3.87 years.

Antral follicle count revealed a significant association with the live birth outcome of fertility treatments. Couples where the female partner had an AFC of less than 5 exhibited lower success rates, with only 9.4% achieving a live birth, compared to 40.0% in couples where the AFC was equal to or greater than 5 ($\boldsymbol{x^2}$= 31.285, df = 1, $p < 0.001$). Semen analysis did not show a significant association with the live birth outcome of fertility treatments. Couples where the semen analysis indicated abnormal results had a live birth rate of 35.9%, while those with normal results had a slightly higher rate of 32.0%. However, this difference was not statistically significant according to the chi-square test ($\boldsymbol{x^2}$= 0.491, df = 1, p = 0.483). Endometrial thickness at the day of ovulation triggering also exhibited a significant association with treatment outcomes. Couples where the endometrial thickness was 7 mm or less had a significantly lower live birth rate of 12.7%, compared to 37.1% in couples where the endometrial thickness was greater than 7 mm ($\boldsymbol{x^2}$= 15.831, df = 1, $p < 0.001$).

Table 8. Infertility profile and biological factors of infertile couples undergone fertility treatments in terms of live birth in Addis Ababa, Ethiopia, 2021-2023.

Variables	**Categories**	**outcome**		x^2**(df)**	**P-value**
		No live birth n(%)	**Live birth n(%)**		
Type of infertility	Primary infertility	152(65)	82(35)	1.188	0.276
	Secondary infertility	124(70.1)	53(29.9)		
Factor of infertility	Female factor	138(69.3)	61(30.7)	3.776(3)	0.287
	Male factor	45(60.8)	29(39.2)		
	Unexplained	86(69.9)	37(30.1)		
	Combined factor	7(46.7)	8(53.3)		
Duration of infertility in years	<5	75(49.7)	76(50.3)	38.122	<0.001
	5-9	118(72.8)	44(27.2)		
	9-14	64(87.7)	9(12.3)		
	≥15	19(76)	6(24)		
AFC	≥ 5	189(60)	126(40)	31.285	<0.001
	<5	87(90.6)	9(9.4)		
Semen analysis	Normal	217(68.0)	102(32.0)	0.491	0.483
	Abnormal	59(64.1)	33(35.9)		
Endometrial thickness	>7	214(62.9)	126(37.1)	15.831	<0.001
	≤7	62(87.3)	9(12.7)		

5.11. Fertility treatment methods and characteristics in terms of live birth

Couples who underwent IVF had a higher live birth rate (38.3%) compared to those who did not undergo IVF (26.5%) (x^2= 6.481, df = 1, p = 0.011). The number of IVF cycles undertaken also exhibited a significant association with treatment outcomes. Couples who underwent multiple IVF cycles had higher live birth rates. Specifically, those undergoing two IVF cycles (63.6%) or three IVF cycles (66.7%) had notably higher live birth rates compared to those undergoing only one cycle (35.0%) (x^2= 14.935, df = 3, p = 0.002). While ICSI showed a trend towards higher live birth rates compared to no ICSI, this association was not statistically significant (x^2= 2.45, df = 1, p = 0.118). Among couples undergoing ICSI, the number of cycles also significantly impacted treatment outcomes. Couples undergoing two cycles of ICSI had a notably higher live birth rate (75.0%) compared to those undergoing only one cycle (34.1%) (x^2= 7.736, p = 0.005). Couples who underwent IUI had a significantly higher live birth rate (23.2%) compared to those who did not (39.3%) (x^2= 11.583, p = 0.001). Similar to IVF and ICSI, the number of IUI cycles also significantly impacted treatment outcomes. Couples undergoing multiple IUI cycles had varying success rates, with those undergoing one cycle having the lowest success rate (11.4%) and those undergoing more than two cycles having higher success rates (x^2= 24.867, p < 0.001). The type of IVF cycle, whether fresh or frozen, showed a significant association with treatment outcomes. Couples undergoing fresh cycles had a higher live birth rate (39.0%) compared to those undergoing frozen cycles (27.3%) (x^2= 6.316, p = 0.012) (Table 9)

Table 9. Description of fertility treatment methods and characteristics of couples who underwent fertility treatments in terms of live birth in Addis Ababa, Ethiopia, 2021-2023

Variables	Categories	Outcome		x^2(df)	P-value
		No live birth n(%)	Live birth n(%)		
IVF	No	139(73.5)	50(26.5)	6.481	0.011
	Yes	137(61.7)	85(38.3)		
Number of IVF cycle	1 cycle	128(65.0)	69(35.0)	14.935(3)	0.002
	2 cycles	8(36.4)	14(63.6)		
	3 cycles	1(33.3)	2(66.7)		
ICSI	No	193(69.7)	84(30.3)	2.45	0.118
	Yes	83(61.9)	51(38.1)		
Number of ICSI cycle	1 cycle	81(65.9)	42(34.1)	7.736	0.005
	2 cycles	3(25.0)	9(75.0)		
IUI	No	150(60.7)	97(39.3)	11.583	0.001
	Yes	126(76.8)	38(23.2)		
Number of IUI cycle	1 cycle	70(88.6)	9(11.4)	24.867(4)	<0.001
	2 cycles	28(71.8)	11(28.2)		
	>2 cycles	28(60.9)	18(39.1)		
Cycle type	Fresh	119(61.0)	76(39.0)	6.316	0.012
	Frozen	157(72.7)	59(27.3)		
Total number of cycles	1 cycle	156(71.2)	63(28.8)	7.14(4)	0.129
	2 cycles	80(66.1)	41(33.9)		
	3 cycles	32(59.3)	22(40.7)		
	4 cycles	6(54.5)	5(45.5)		
	5 cycles	2(33.3)	4(66.7)		

5.12. Fertility treatment outcome in terms of live birth

One third 136(33.1%) of the total 411 couples, or 136(70.5%) of the couples who achieved clinical pregnancy, had achieved live birth. From the 136 couples who achieved live birth, singleton babies have predominated by having a count of 123(91.1%). Twin births accounted for 10(7.4%) and triplet births were 2(1.5%). From the 57(29.5%) who had lost their pregnancy, 52(91.2%) of them lost their fetus at the first trimester, and 5(8.8%) had second trimester pregnancy loss. 10(2.4%) couples were lost to follow up.

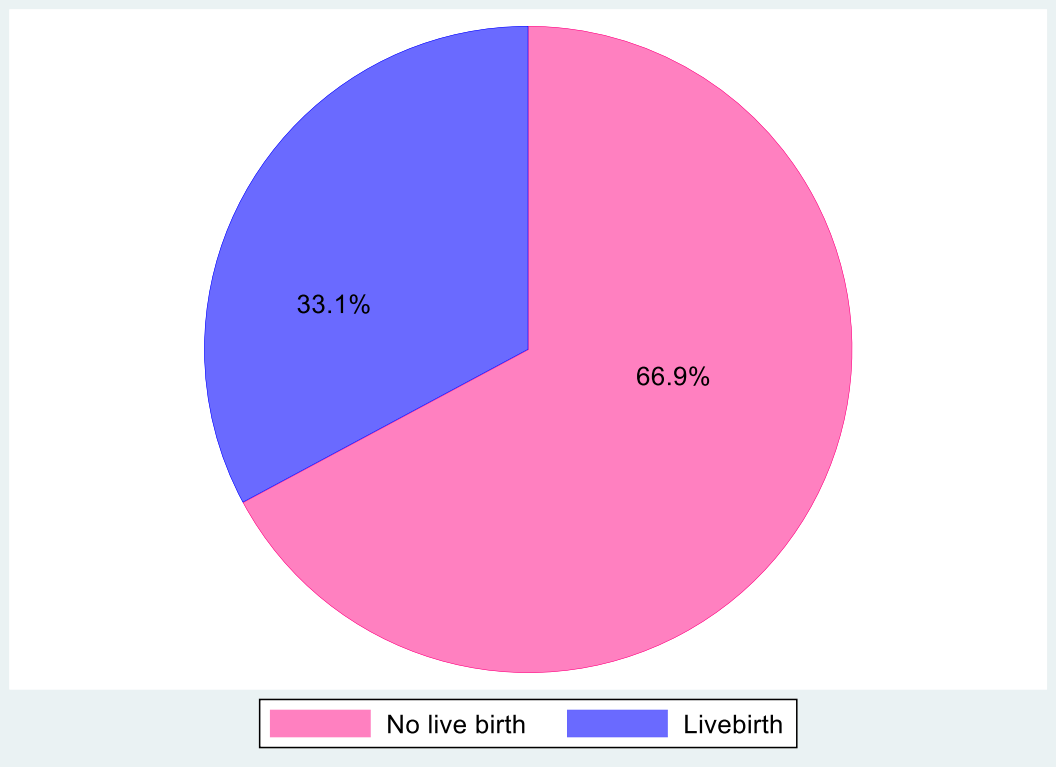

Figure 5. Live birth outcome of ART among couple who underwent assisted reproductive technology in Addis Ababa, Ethiopia, 2021-2023

5.13. The overall Kaplan-Meier survival curve estimate

The Kaplan-Meier curve for overall survival represents the probability of achieving a live birth over time among women undergoing Assisted Reproductive Technology (ART) procedures (Figure 6). From the curve, we can visualize that no live birth occurred until around month 9 from the start of ART procedure and there seems to be a significant number of live births on around 10^{th} month. Again, occurrence of live birth increases up to around 14^{th} month, where it starts to decline again. The probability of survival, which is the likelihood of not having a live birth tend to decrease over time throughout the follow-up period. For instance, at interval 8-12 months the probability of not achieving live birth is 0.7875, indicating that approximately 78.75% of the couple had not yet experienced live birth by the end of this interval (Table 6). The earlier time intervals (4-8 months and 8-12 months) the decline in the survival probability appears to be more pronounced compared to later intervals. This suggests that the majority of live births occur within the earlier stages of the follow-up period. Towards the later intervals, the likelihood of achieving a live birth tend to stabilize, which may indicate that after a certain

duration of ART treatment the likelihood of achieving a live birth reaches a relatively steady state.

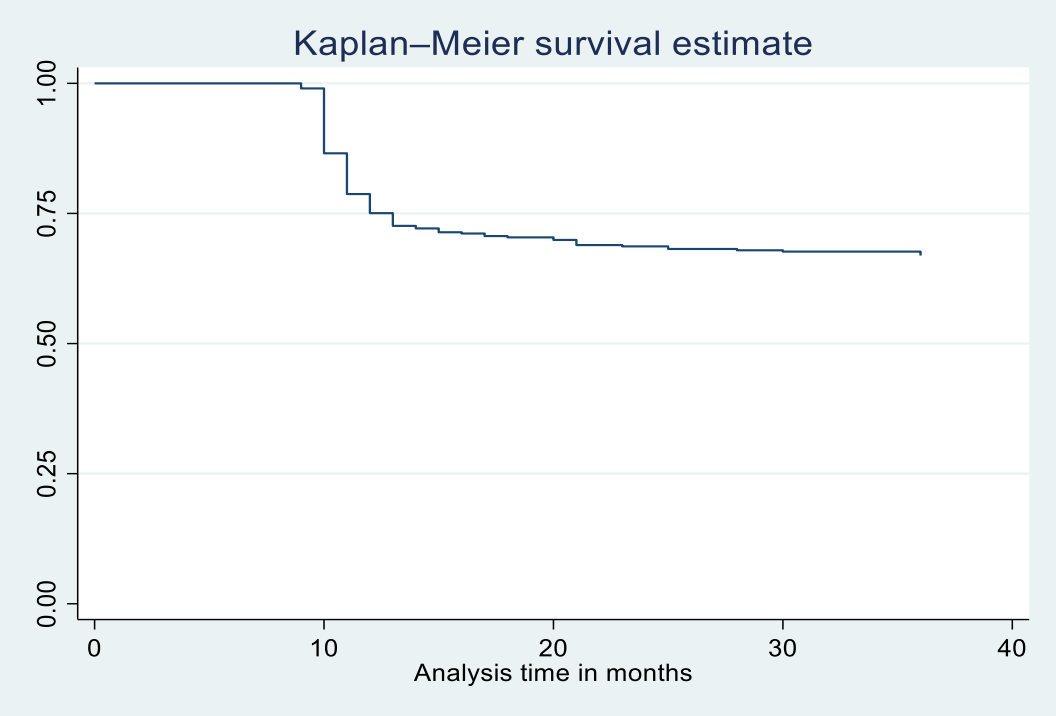

Figure 6. The overall Kaplan-Meier survival curve of infertile couple undergoing fertility treatments in Addis Ababa

Table 10. Life table of infertile women who underwent assisted reproductive technology in Addis Ababa, Ethiopia, 2021-2023

Time in months	Beg. Total	Event (live birth)	Censored	Probability of survival	Standard error	95% CI
4-8	411	0	1	1.0000	0.0000	..
8-12	410	87	1	0.7875	0.0202	0.7447, 0.8241
12-16	322	30	1	0.7141	0.0223	0.6676, 0.7552
16-20	291	4	2	0.7042	0.0226	0.6574, 0.7459
20-24	285	7	3	0.6868	0.0229	0.6394, 0.7294
24-28	275	2	2	0.6818	0.0231	0.6342, 0.7246
28-32	271	2	0	0.6768	0.0232	0.6290,0.7198
36-40	269	3	266	0.6618	0.0242	0.6120, 0.7068

5.14. Kaplan- Meier survival graphs for selected predictors

As the Kaplan-Meier survival curves show in Figure 7, Age of the woman being below 35 years of age, AFC count of 5 and above, IVF being the type of ART taken, having more treatment

cycles, having fresh treatment cycles and having male factor infertility were observed to have low survival or higher live births while, age 35 and above, AFC below 5, having IUI or combined IUI and IVF, fewer treatment cycles, frozen type of cycles and not having male factor infertility tend to have higher survival or lower live births.

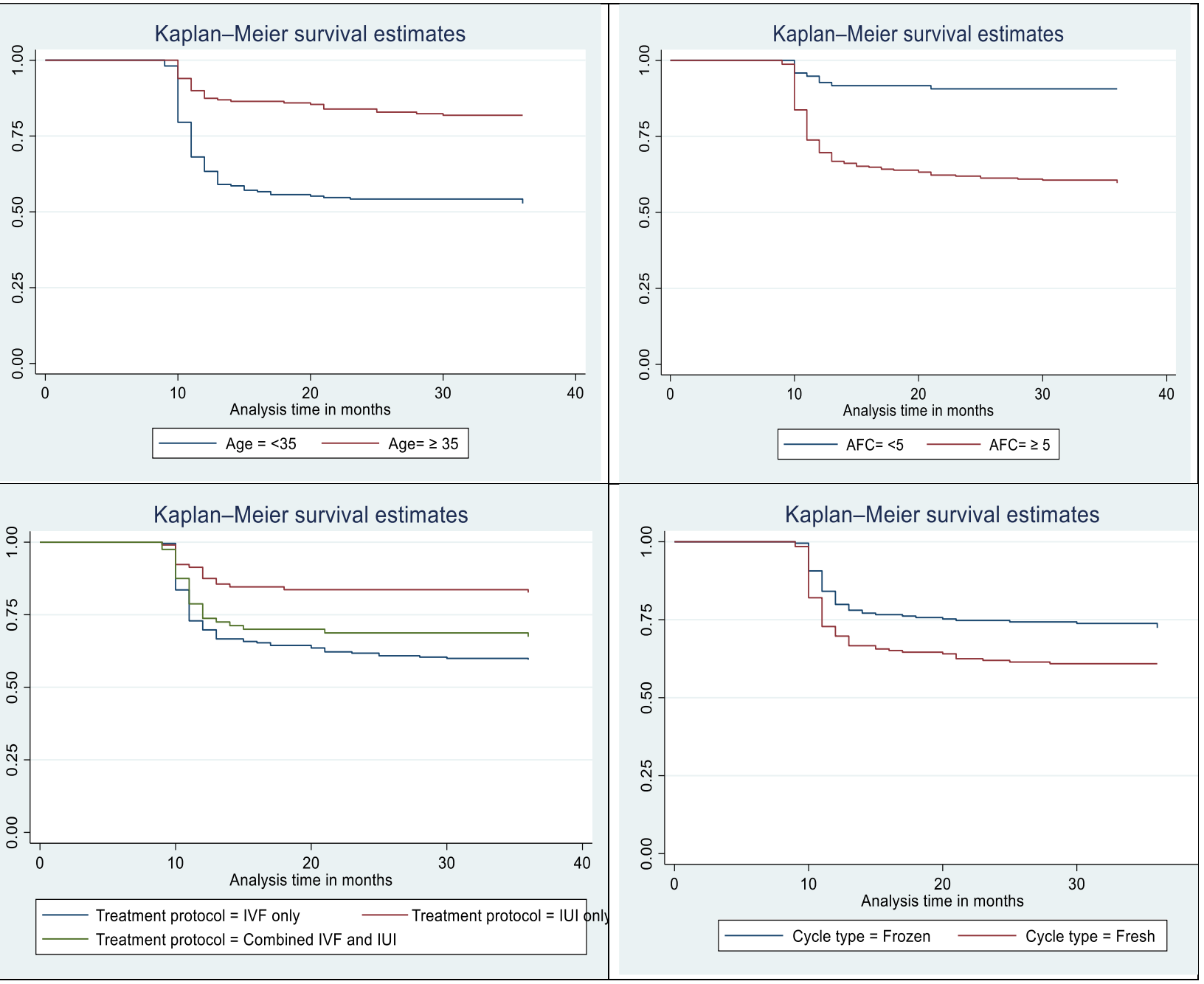

Figure 7. Kaplan-Meier survival estimates for selected predictors

The log-rank test was employed to assess the differences in survival distribution among various categories of covariates in infertile couple undergoing ART treatments. Significant differences in survival distributions were observed for Age (x^2 = 40.86, p < 0.0001), surgical history (x^2 = 3.96, p = 0.0465), AFC (x^2= 29.15, p < 0.0001), Cycle type (x^2= 6.81, p = 0.0091) and other variables, however no significant differences in survival distributions were found for the total number of cycles, male factor infertility, combined factor infertility, total number of cycles, and laparoscopy status (p > 0.05) (Table 7).

Table 11. log rank test for equality of survival function of live birth among infertile women couple who underwent assisted reproductive technology in in Addis Ababa, Ethiopia, 2021-2023

Variables	**Category**	**Observed Events**	**Expected Events**	x^2 **test**	**Pr>**x^2
Age	<35	99	63.47	40.86	<0.0001
	≥35	36	71.53		
Duration of infertility in years	<5	76	44.70	39.78	<0.0001
	5-9	44	54.98		
	10-14	9	26.30		
	≥15	6	9.02		
Surgical history	No	118	109. 26	3.96	0.0465
	Yes	17	25.74		
Underlying health conditions	No	125	114.58	6.77	0.0093
	Yes	10	20.42		
HTN	No	133	126.36	5.88	0.0153
	Yes	2	8.64		
TB	No	130	132.58	3.05	0.0809
	Yes	5	2.42		
Male factor	No	106	111.37	1.60	0.2052
	Yes	29	23.63		
Combined factor	No	127	130.34	2.70	0.1006
	Yes	8	4.66		
Endometrial thickness	>7mm	126	109.30	14.49	0.0001
	≤7mm	9	25.70		
AFC	<5	9	35.55	29.15	<0.0001
	≥5	126	99.45		
Treatment protocol	IVF	91	71.72	16.22	0.0003
	IUI	18	37.05		
	Both	26	26.23		
Total number of cycles	1 cycle	63	74.10	7.18	0.1265
	2 cycles	41	39.00		
	3 cycles	22	16.75		
	4 cycles	5	3.21		
	5 cycles	4	1.93		
Cycle type	Frozen	59	73.51	6.81	0.0091
	Fresh	76	61.49		
Laparoscopy	No	132	128.38	2.25	0.1339
	Yes	3	6.62		

Footnote: **HTN**: Hypertension; **TB**: Tuberculosis; **AFC**: Antral follicle count

5.15. Factors associated with live birth among infertile women undergoing ART treatment

Women aged ≥35 demonstrated a 63% lower hazard of achieving a live birth compared to those aged <35 (AHR = 0.63, 95% CI: 0.40-0.99, p = 0.047). Longer duration of infertility was associated with decreased adjusted hazards of live birth. Specifically, women with infertility durations of 5-9 years (AHR=0.59, CI: 0.39- 0.896) and 10-14 years (AHR=0.46 CI: 0.22- 0.98) exhibited lower hazards of live birth compared to those with durations <5 years.

Women undergoing intrauterine insemination (IUI) had significantly lower adjusted hazards of live birth compared to those undergoing in vitro fertilization (IVF) (AHR = 0.48, 95% CI: 0.27-0.85, p = 0.011) which is a decrease of 48%. Increasing the total number of ART cycles was associated with higher hazards of live birth. Notably, women undergoing 4 cycles (AHR = 3.02, 95% CI: 1.09- 8.35, p = 0.033) or 5 cycles (AHR=4.06, 95% CI: 1.28- 12.88, p=0.017) had significantly higher hazards of live birth compared to those undergoing only one cycle. Fresh embryo transfer was associated with 1.5 times higher hazards of live birth compared to frozen embryo transfer (AHR = 1.57, 95% CI: 1.11-2.22, p = 0.012).

Table 12. Bivariable and Multivariable cox regression survival model analysis for predictors of live birth among couples who underwent assisted reproductive technology in Addis Ababa, Ethiopia, 2021-2023

Variables	Categories	Status		CHR (95%CI)	AHR (95% CI)	P-value
		Censored n (%)	Event n (%)			
Age	<35	112(40.6)	99(73.3)	**Ref**	**Ref**	
	≥35	164(59.4)	36(26.7)	0.32 (0.22- 0.47)	0.63 (0.40- 0.99)	**0.047***
Duration of infertility in years	<5	75(27.2)	76(56.3)	**Ref**	**Ref**	
	5-9	118(42.8)	44(32.6)	0.47 (0.32- 0.68)	0.59 (0.39- 0.896)	**0.013***
	10-14	64(23.2)	9(6.7)	0.20 (0.10-0.39)	0.46 (0.22- 0.98)	**0.043***
	≥15	19(6.9)	6(4.4)	0.39 (0.17- 0.89)	1.23 (0.49- 3.09)	0.654
Surgical history	No	218(79)	118(87.4)	**Ref**	**Ref**	
	Yes	58(21)	17(12.6)	0.61 (0.37- 1.02)	0 .85 (0.495- 1.46)	0.549
Underlying health conditions	No	229(83)	125(92.6)	**Ref**	**Ref**	
	Yes	47(17)	10(7.4)	0.45 (0.24- 0.85)	0.53 (0.16- 1.72)	0.295
HTN	No	255(92.4)	133(98.5)	**Ref**	**Ref**	
	Yes	21(7.6)	2(1.5)	0.22 (0.05-0.89)	0 .64 (0.11- 3.90)	0.632
TB	No	273(98.9)	130(96.3)	**Ref**	**Ref**	
	Yes	3(1.1)	5(3.7)	2.11 (0.86- 5.15)	4.06 (0.92- 17.94)	0.064
Male factor	No	231(83.7)	106(78.5)	**Ref**	**Ref**	
	Yes	45(16.3)	29(21.5)	1.29 (0.86-1.95)	1.19 (0.77- 1.83)	0.440
Combined factor	No	269(97.5)	127(94.1)	**Ref**	**Ref**	
	Yes	7(2.5)	8(5.9)	1.76(0.86- 3.60)	1.47 (0.70- 3.09)	0.305
Endometrial thickness	>7mm	214(77.5)	126(93.3)	**Ref**	**Ref**	
	≤7mm	62(22.5)	9(6.7)	0.30 (0.15- 0.59)	0.54 (0.27- 1.10)	0.093
AFC	<5	87(31.5)	9(6.7)	**Ref**	**Ref**	
	≥5	189(68.5)	126(93.3)	5.02 (2.55- 9.88)	3.31 (1.60- 6.86)	**0.001***
Treatment protocol	IVF	136(49.3)	91(67.4)	**Ref**	**Ref**	
	IUI	86(31.2)	18(13.3)	0.38 (0.23- 0.63	0.48 (0.27- 0.85)	**0.011***
	Both	54(19.5)	26(19.3)	0.78 (0.50- 1.21)	0.61 (0.36- 1.04)	0.068
Total number of cycles	1 cycle	156(56.5)	63(46.7)	**Ref**	**Ref**	
	2 cycles	80(29)	41(30.4)	1.24 (0.83- 1.83)	1.34 (0.88- 2.07)	0.172
	3 cycles	32(11.6)	22(16.3)	1.55 (0.95- 2.51)	1.68(0.94- 2.99)	0.077
	4 cycles	6(2.2)	5(3.7)	1.83 (0.74- 4.56)	3.02 (1.09- 8.35)	**0.033***
	5 cycles	2(0.7)	4(3)	2.43 (0.89- 6.69)	4.06 (1.28- 12.88)	**0.017***
Cycle type	Frozen	157(56.9)	59(43.7)	**Ref**	**Ref**	
	Fresh	119(43.1)	76(56.3)	1.54 (1.096- 2.17)	1.57 (1.11- 2.22)	**0.012***
Laparoscopy	No	260(94.2)	132(97.8)	**Ref**	**Ref**	
	Yes	16(5.8)	3(2.2)	0.44 (0.14- 1.38)	0.65 (0.199- 2.13)	0.477

Footnote: **Ref:** Reference category; **HTN**: Hypertension; **TB**: Tuberculosis; **AFC**: Antral follicle count

5.16. Assumption checking for Cox proportional hazards model

The Global test for Schoenfeld residuals indicated that the overall Cox proportional hazards model meets the assumption of proportionality (x^2=24.22, p=0.2329). The test was also performed for each covariate included in the Cox proportional hazards model. For each variable, the test results indicated no significant violation of the proportionality assumption (p>0.05), suggesting that the hazard ratios associated with these variables remain constant over time. Additionally, the cox-Snell residual graph was plotted against the estimated cumulative hazards rate. It is observed that the plot closely follows a 45-degree line indicating an agreement with the theoretical exponential form. This alignment between the observed cumulative hazards of the residuals and the expected cumulative hazards under the model indicated that the model captures the underlying survival patterns effectively (Figure 8)

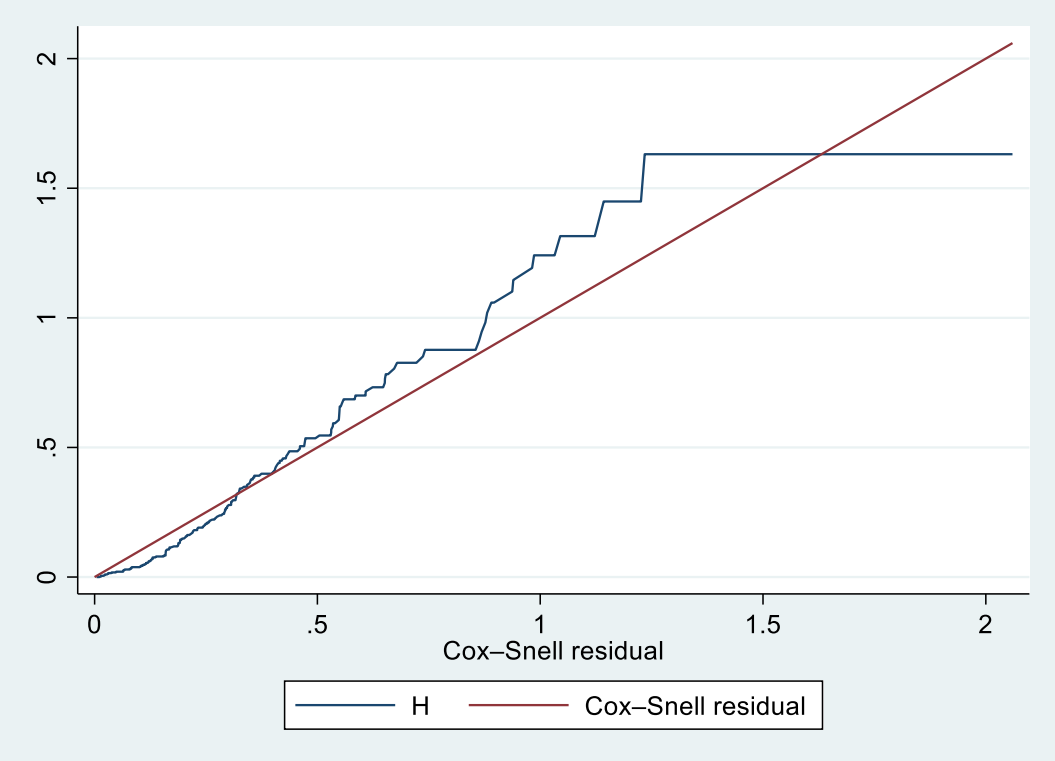

Figure 8: Cox-residual assumption graph for overall model fitness

6. Discussion

This study reports the success rate of fertility treatments and time-to-live birth of those treatments considering various possible influencing factors among couples who underwent fertility treatments at public and private fertility centers of Addis Ababa.

From the total 411 couples who underwent fertility treatments, 47% of them achieved successful clinical pregnancy. The cumulative clinical pregnancy rate of IVF after a maximum of three cycles, despite the fertilization protocol, was found to be 70.6% in our study, which is similar to a study conducted in Tokyo (66.7%) (57).

The success rate of IVF/ICSI in this study was found to be 39.3% per cycle, where both types of insemination methods, which are conventional IVF and ICSI, have similar clinical pregnancy rates per cycle (39.2 and 39.4% respectively). This finding is in line with a previously conducted study in the USA with 39.8% pregnancy rate (58), but appears to have a higher clinical pregnancy rate than a previously conducted study in St. Paul's Hospital Millennium Medical College (SPHMMC) with a clinical pregnancy rate of 30.1% (31). This discrepancy could be a result of changes in treatment technologies and techniques over time since the previous study was conducted five years back and in only one fertility center.

The cumulative pregnancy rate of IUI in our study was found to be 21.9%, which is consistent with a finding of a study done in Italy with data from 1997-2017 which reported 21.89% (33). The clinical pregnancy rate on the other hand was found to be 12% per cycle.

Women aged below 35, were found to be four times more likely (AOR= 4.016; 95% CI: 2.292, 7.036) to have a successful clinical pregnancy from fertility treatments than those aged 35 and more. This finding goes hand in hand with reports of studies conducted in Addis Ababa, Greece, Iran and China (31,35,36,59). This relationship could be accounted for by the presence of high ovarian reserve in women under the age of 35 compared to women 35 years of age and above. On the contrary, a study conducted in Namibia revealed a higher success rate of IVF treatments among women aged above 49 compared to the younger age groups (37). This unexpected finding may be attributed to the fact that the women in the above-49 age group in that specific study underwent a minimum of two cycles of treatment, potentially increasing their odds of success

through repeated attempts. the importance of age in fertility treatment success should be given emphasis to patients, potentially encouraging earlier interventions.

Cause of infertility may affect treatment outcomes significantly. Tubal factor infertility was found to have a significant association with the likelihood of achieving clinical pregnancy, with the presence of tubal factor infertility decreasing the odds of a successful clinical pregnancy by 58%. This finding is supported by a study in Iran that reported high risk of poor fertilization among women with tubal disease (59). Another review of studies on IUI outcome supports the above finding in which tubal factor infertility appears to be associated with the lowest clinical pregnancy rate (PR) after IUI (42). This low success rate may be attributed to structural abnormalities and mechanical barriers in the fallopian tubes. These issues hinder the interaction between sperm and egg, making fertilization less likely. Moreover, they compromise the environment necessary for embryo implantation, further reducing the chances of success with IVF and IUI.

Longer duration of infertility was found to be significantly associated with poor clinical pregnancy outcome in this study, a single year increase in duration of infertility would have a 15% decrease in the odds of PR. This finding is supported by multiple studies, such as a study conducted in Iraq which studied the relationship between duration of infertility and outcomes of IUI among infertile men and reported that duration of below 4 years has the most favorable success, whereas duration of 10 years and above has the least chance of success (40). Another study in Iran also supports this evidence by showing that longer duration of infertility is associated with decreased PR (60). This relationship could be attributable to the increasing age of the couple as the duration also increases. This can interfere with the ovarian reserve and sperm quality. But still now the reason for this relationship between duration of infertility and PR of fertility treatment is not well understood and needs further research.

Having high AFC count (≥5) appears to be associated with higher chance of achieving clinical pregnancy after fertility treatments. Similarly, a study conducted in China also found that with an increasing number of antral follicles increased the CPR (61). Higher AFC count indicates better ovarian reserve and ovarian response to stimulation, which in turn may increase the chance of clinical pregnancy. On the other hand, a study conducted in Addis Ababa reported that increased AFC count is significantly associated with a better ovarian response but found no association

with PR (31). AFC can be used as a key diagnostic tool to evaluate ovarian reserve and guide treatment plans. Patients with low AFC may need more intensive ovarian stimulation protocols or alternative approaches such as donor eggs.

Another predictor of clinical pregnancy was endometrial thickness at the day of ovulation triggering. Women whose EMT>7mm were 3 times more likely to achieve clinical pregnancy compared to women with EMT≤7mm. A systematic review and meta-analysis study supports this finding in which thin endometrial thickness (≤7mm) appeared to be associated with significantly lower odds of clinical pregnancy by 58% after IVF (44). Another study in Japan which studied the fertility outcomes of women undergoing ART after they went through treatment for endometrial cancer reported that the implantation rate for women with thin endometrium was lower (57). A study in Iran supported the above findings in that CPR of IVF/ICSI and IUI tends to increase as EMT increases until it reaches 10mm, where it starts to decline again (60). This may be accounted for the endometrial receptivity, however more research is needed to clarify the relationship further. Monitoring and optimizing endometrial thickness should be an integral part of fertility treatments.

For every increase in one cycle of treatment, there appears to be 1.8 times increased odds of successful clinical pregnancy success (AOR= 1.826; 95% CI: 0.784, 0.922). This finding goes in line with a study in Germany that reported an increase of CPR as the number of ART cycles increased and it reached 100% after 18 treatment cycles (53). Patients should be counseled about the potential need for multiple cycles to achieve success. Setting realistic expectations and providing emotional support for multiple cycle attempts can improve patient compliance and outcomes.

This study found the cumulative live birth rate of the treatments to be 33.1%, which is comparable with a study done in China on women of age 35 and more, which found 32.12% live birth rate with ART cycles going up to a maximum of 6 (62).

When we look at separate live birth outcomes of the different fertility treatments, the cumulative live birth rate of IVF was 27.5% in this study, which is much lower than the study conducted in Tokyo which reported 59.5% (57). The cumulative live birth rate of IVF after the first complete cycle was 31.1%, which is supported by studies conducted in the UK and Australia, which presented live birth after the first complete cycle of IVF to be 29.5 and 37.5% respectively

(54,63). However, it appears to be higher than a study in the USA with 17.8% (58). This could be the result of the difference in the age of the women in the studies, since the study in the USA only included women aged 40 and above. Live birth of IVF at the second cycle in our study was 62.2% which is much higher than the UK study which reported 22.8% (54). This could be because of the very small number of couples in our study who tried for a second cycle of the IVF treatment which is only 37 couples. The cumulative live birth rate of IUI was 23.2%, which is found to be much higher than a study in Italy with data from 1997-2017, which reported 17.58% (33).

Multiple birth rates from a total of 135 live births account for 8.9%, which is comparable to the Australian study that reported 7.5% (63). This finding appears to be much lower than a review of Assisted reproductive technology which reported multiple births to be above 20% in sub-Saharan African countries (64). This lower multiple birth rate is considered a good success since multiple pregnancy and births are considered to be high risk. Maintaining low multiple birth rates is crucial for minimizing risks to both mother and infants. When we consider another outcome of clinical pregnancy other than live birth, the rate of pregnancy loss after the first cycle was 14% in our study, most occurring in the first trimester, which is higher than the study in the UK which presented to be around 8.3% (54). This finding underscores the need for close monitoring and support during early pregnancy in ART patients.

This study showed a decrease in cumulative live birth rate (CLBR) in the age group ≥35 years compared to <35, where there was a 63% decrease in live birth. This is generally in agreement with other studies that assessed the impact of age in live birth outcome of ART treatment (54,62). As the age of women increases, especially for women 35 years and above, fertility rate and live birth rate through ART tend to decrease. Pregnancy comorbidities and abortion increases as well (62).

Longer duration of infertility was associated with unfavorable outcome of live birth in this study, where couples with longer duration have decreased hazard of live birth compared with shorter durations. This finding appears to be in line with other studies (40,54,65). Longer duration of infertility is associated with advanced age, and age-related decline in pregnancy, hence the decrease in live birth outcome. Early intervention is crucial and couples should be advised not to delay seeking fertility treatments.

Couples who underwent IUI had a 48% decrease in hazard of live birth compared to couples who underwent IVF as their fertility treatment. This finding is supported by other studies that also found substantially higher live birth rate among couples who took IVF than IUI (66). IVF involves fertilizing the eggs and sperm in a controlled environment in the laboratory, and then the transfer of resulting embryos into the uterus. This allows for more direct control over the fertilization process and the selection of high-quality embryos for transfer. This may potentially increase the chances of successful implantation and live birth in the process of IVF compared to IUI. In IUI, fertilization occurs within the uterus or the fallopian tubes. Additionally, IVF is usually recommended for couples with more complex infertility issues, such as tubal blockages, severe male factor infertility, or advanced maternal age rather than IUI, which may have lower chances of success with IUI alone. On the other hand, IUI is typically recommended for couples with less severe infertility issues, such as mild male factor infertility or unexplained infertility. In IVF, the most motile and viable sperm are selected for, which may improve the chances of successful fertilization and embryo development compared to IUI, whereas in IUI, sperm are simply washed and prepared before insemination. These factors may possibly contribute to this significant difference in live birth rate between these two treatments.

Each treatment cycle was summed up and analyzed against the live birth outcome from the overall ART treatment where the maximum treatment cycle being 5 cycles. The result showed that couples who underwent 4 or 5 cycles of ART had a significant increase in the hazards of live birth compared to couples who had only one cycle of ART. This holds true for another study in Australia where cumulative live birth increased as treatment cycles increased to the maximum of 5 cycles in IVF treatment (63). Another study in China contradicts this finding where it was reported that the highest live birth rate was found in the first two cycles, and live birth rate significantly decreased after the second cycle (67). This study was conducted on women with poor ovarian response, which may result in fewer eggs retrieved and lower embryo yield, which may negatively affect the chances of successful pregnancy consecutively affecting the live birth outcome.

A study conducted in Iran reported that frozen cycles were associated with greater live birth outcomes compared to fresh treatment cycles in IVF (68). Similar findings were reported in another study where frozen ART cycles were 1.26 times (AHR= 1.26, CI: 1.02 – 1.55) more

likely to have live birth compared to fresh cycles. However, frozen cycles were more associated with increased hazards of early miscarriage (69). Our study's results showed that fresh cycles were associated with 1.5 times the hazard of having live birth compared to frozen cycles. This relationship between cycle type and live birth outcome needs more investigation with future research.

7. Strength and limitation of the study

Strength of the study

The strength of this study lies in its comprehensive and inclusive design. By incorporating data from both IVF/ICSI and IUI treatments, the research provides a broad overview of infertility treatment outcomes. By including data from both private and public centers, it ensures that the findings are representative of the potentially diverse healthcare settings in between public and private centers in Addis Ababa, which enhances the generalizability of the results. Additionally, the use of both logistic regression analysis and survival analysis offers a robust statistical framework, which allows for the identification of key predictors of clinical pregnancy and the examination of time to live birth, respectively. This dual-method approach enhances the depth and reliability of the findings, offering valuable insights for improving infertility treatments.

Limitation of the study

The study mainly relied on patient information from medical charts, which is prone to missing data. Because of that, it was a challenge to get full patient information on the charts on some variables such as Body mass index, hormonal parameters of the patients and some sociodemographic characteristics such as income and educational background. For this reason, our study lacked to assess the association between those variables to the outcome of fertility treatments. Another limitation is accessibility issues associated with the phone interview. Poor network connection and drop calls interrupted the flow of the interview.

8. Conclusion and recommendation

8.1. Conclusion

This study provides a comprehensive analysis of infertility treatment outcomes in Ethiopia, examining both IVF/ICSI and IUI across private and public healthcare settings in Addis Ababa. This study has identified the success rate of infertility treatments in terms of both clinical pregnancy and live birth, key predictors of clinical pregnancy and explored the time to live birth, offering a robust statistical understanding of treatment success. A clinical pregnancy was achieved by forty seven percent and a live birth was realized by thirty three percent. Couples who underwent IVF procedures were found to have higher clinical pregnancy rate per cycle compared to couples with IUI. Younger women, and couples with several treatment cycles also tend to have better chances at achieving clinical pregnancy and live birth outcomes from ART.

Even though the prevalence of secondary infertility was reported to be higher in Ethiopia, most women in our study were with primary infertility and below 35 years of age, which may indicate that the treatment seeking behavior of these groups exceeds their counter others. Therefore, stakeholders may involve in creating awareness about these treatments. The clinical pregnancy rate, live birth outcomes and factors that are associated with these seem to be in line with majority of the studies. This may show that there is a promising ART treatment here in Ethiopia that is comparable with the other part of the world. The clinical significance of these findings lies in their potential to guide health care providers in optimizing ART treatments and improving outcomes for patients undergoing fertility interventions.

8.2.Recommendation

For Ministry of Health: Early intervention for couples suffering from infertility should be given emphasis, specially to prevent age related decline in fertility and to enhance the chances of successful fertility treatments.

For policy makers: we recommend to allocate resources to support expansion and enhancement of fertility services including ART in Addis Ababa and regional hospitals, to make these services more affordable and accessible. Launch public awareness campaigns to educate the community

about fertility issues, available treatment options, and the importance of seeking fertility care early.

To practitioners: While the total number of treatment cycles showed positive associations with treatment success, clinicians should balance the benefits of additional treatment cycles with possible individual burdens. Shared decision making between healthcare providers and patients is essential to determine the optimal treatment repetition for each individual couple.

To patients: The findings of this study suggest that fertility treatment outcomes in fertility centers in Addis Ababa are comparable to those reported in studies conducted worldwide. Therefore, we recommend patients consider seeking treatment at these centers. The comparable outcomes imply that patients can expect quality care and effective fertility interventions locally, reducing the need for seeking treatment abroad.

To researchers: Continued research in fertility treatment modalities, predictive factors and advancements in ART technologies is needed to further improve the treatment outcome and address the diverse needs of the patients undergoing these treatments. We recommend researchers conduct prospective studies with long term follow up which enables researchers track treatment outcomes and pregnancy trajectories over time.

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ANNEX I: Information sheet and consent form

Addis Ababa University

College of Health Science, School of Public Health

Introduction:

Thank you for considering participating in this study. This information sheet is designed to provide you with details about the research project titled Success rate and time-to-live birth of fertility treatments among couple attending fertility centers in Addis Ababa, Ethiopia" led by Principal Investigator Saron Kasahun. Please listen carefully and ask any questions about the study before you agree to join. You may ask questions at any time after joining the study

Objective of the Study:

The study aims to determine the magnitude of treatment success on infertility treatment, identify the time to live birth of infertility treatments and identify factors influencing treatment success among couple who have undergone fertility treatments.

Ethical Considerations:

You will be provided with detailed information about the study, and your oral consent will be sought before participation. Your participation is entirely voluntary, and you can withdraw at any point without consequence. Your identity will be kept confidential.

Benefits and risks of Participation:

By participating, you will contribute valuable insights that may enhance our understanding of the success and the time it takes for the success of infertility treatments. We don’t anticipate that there are any risks associated with your participation.

Contact Information:

If you have any questions or concerns about the study, please feel free to contact the Principal Investigator, Saron Kasahun, using the following:

- **Phone Number**: +251939364694

- **Email**: saronk52@gmail.com

Or Dr. Zeytu Gashaw Asfaw

- **Phone Number:** +251911877543
- **Email:** zeytugas@gmail.com

Can I proceed to the questions now?

Yes ---------- Proceed

No ---------- Stop

Name of Data collector: _____ Signature of the Data collector _____ Date: _____ Time _____

ANNEX II: Waiver of consent

From: Saron Kasahun [*Date*]

To: ———————————————————

Dear Chair,

This letter is to request a waiver of ethical clearance for a study on "Success rate and time-to-live birth of fertility treatments among couple attending fertility centers in Addis Ababa, Ethiopia" that will be conducted for the partial fulfillment for the degree of Masters of Public Health in Epidemiology and Biostatistics specialty from Addis Ababa University. The data used will be collected from patient's medical chart from the two centers.

The study is done by Saron Kasahun as the Principal Investigator. The purpose of the study is to measure the success of infertility treatment and analyze the effects of factors in relation to the success. Additionally, we will identify the time to success until pregnancy is achieved.

I would like to kindly request the Research Ethical Committee for a waiver of informed consent for this study for the following reasons:

1. **The research involves minimal risk**, as the review of subjects' medical records is for limited information. the data are derived from clinically indicated procedures. There is an extremely low probability of harm to subjects. The precaution taken to limit the record review to specified data and double coding of the data further minimize the major risk, which is breach of confidentiality. Contacting subjects to obtain their consent could be considered an invasion of privacy and may cause subjects undue anxiety.

2. **The rights and welfare of the individual would not be adversely affected** because the treatment procedures were already completed, or would be completed, regardless of the research. None of the results of the research would affect the clinical decisions about the individual's care because the results are analyzed after the fact. Subjects are not deprived of clinical care to which they would normally be entitled.

3. **The research could not be practicably carried out without a waiver**. Identifying and contacting the hundreds of potential subjects, although not impossible, would not be feasible for a review of their medical records for information that would not change the care they would already have received.

4. **The data will be anonymized and be stored in a safe place**. The data will be collected from patient's medical chart. It is completely anonymous and will be kept in a password-protected folder. The data is solely accessible to the study team.

I hope to have informed you sufficiently on the objective and content of this study to make a decision on my request.

Yours sincerely,

Saron Kasahun

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St. Paul's Hospital Millennium Medical College
የስነተዋልዶ ማዕከል
Center for Reproductive Medicine

Date: 29/02/2024

Re: Approval of Waiver of Informed Consent

Dear Saron Kasahun,

I am writing to inform you that your request for a waiver of informed consent for your research study titled "Success rate and time-to-live birth of fertility treatments among couples attending fertility centers in Addis Ababa, Ethiopia" has been approved. After careful consideration of your proposal, it has been determined that your study meets the necessary criteria for such a waiver.

This decision is based on the following considerations:

1. **Minimal Risk**: Your study involves no more than minimal risk to participants.
2. **Protection of Rights and Welfare**: The waiver will not adversely affect the rights and welfare of the participants involved.
3. **Impracticability of Conducting the Research Without the Waiver**: It has been established that the research could not practicably be carried out without the waiver.
4. **Provision of Pertinent Information**: Whenever appropriate, participants will be provided with additional pertinent information after their participation in the study.

This approval is granted with the understanding that you will conduct the research in strict adherence to the protocol you have submitted. Any deviations or modifications to the study protocol must be promptly reported and approved.
Your commitment to maintaining the highest standards of ethical research is greatly appreciated. Should you encounter any issues or require further clarification, please do not hesitate to contact my office.
We are confident that your study will contribute valuable insights and advancements in the field while upholding the ethical standards of our institution.

Sincerely,

ዶ/ር መሰረት አንሳ
ዋና ስራ አስኪያጅ
Dr Meseret Ansa
C.E.O of CFRM SPHMMC

[Dr. Meseret Ansa,

CEO of Center for Fertility and Reproductive Medicine

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in reply please refer to our ref No

ANNEX III: Data abstraction format

No	Variables	Description	skip
Part I: Socio demographic characteristic			
Questionnaire number—————————		Health facility 1. SPHMMC **2.** Ethio fertility and IVF	
101.	Age (Years)	-	
102.	Residence	1. Addis Ababa 2. Out of Addis Ababa 3. Out of Ethiopia	
103.	Underlying health conditions	1. Yes 2. No ⟶	**Skip to 105**
104.	If yes,	1. Thyroid disorder 2. Endocrine disorder 3. Autoimmune disease 4. HIV/AIDS 5. Cardiac 6. kidney disease 7. DM 8. HTN 9. STIs 10. Other—————	
105.	Surgical history	1. Yes 2. no ⟶	**Skip to 107**
106.	If yes,	1. Pelvic or abdominal 2. Ovarian or fallopian tube 3. Other—————————	
Part II: Infertility treatment information			

201.	Type of Infertility	1. Primary infertility 2. Secondary infertility	
202.	Factor of infertility	1. Female factor 2. Male factor 3. Combined 4. Unexplained	
203.	Infertility etiology	Specify the cause of infertility————————————————	
204.	Duration of infertility (In years)	-————————————————	
205.	Date of **start** of treatment (DD/MM/YY)	_____ /_____ /_____ G.C.	
206.	Type of infertility treatment given	1. IVF 2. ICSI 3. IUI	
207.	Cycle type	1. Fresh 2. Frozen	
208.	Number of treatment cycles	1. IVF_____ 2. ICSI_____ 3. IUI_____	
209.	Surgical procedure for infertility	1. Yes 2. No ⟶	**Skip to 301**
210.	If yes, specify type of surgery (Specify)	_____	
Part III: Clinical and Laboratory Data			
301.	Antral follicle count	————————————————	
302.	Semen Analysis	1. Normal 2. Abnormal	

303.	Endometrial thickness (mm)	————————————————	
Part IV: Outcome			
401.	Treatment Outcome confirmed after HCG test or ultrasonography	1. Successful clinical pregnancy ⟶ 2. No pregnancy ⟶	**Go to questionnaire** **End**

ANNEX IV: Questionnaire

no	Question	Response	Skip
1.	What was the outcome of the pregnancy?	1. Live birth 2. Pregnancy loss →	Skip to no 4
2.	When was the date delivery? (DD/MM/YY)	—/—/——G.C.	
3.	What was the outcome of the live birth?	1. Singleton 2. Twin 3. Triplet 4. Other(specify)————	
4.	At what month did pregnancy loss happen?	1. First 3 months 2. 3-6 months 3. After 6th month	

ANNEX V: Information sheet, consent form and questionnaire - Amharic

የመረጃ መስጫ ገጽ እና የስምምነት መግለጫ ቅጽ

መግቢያ፡-

በጥናታችን ውስጥ ለመሳተፍ ስላሰቡ እናመሰግናለን። ይህ የመረጃ ወረቀት የተዘጋጀው በዋና መርማሪ ሳሮን ካሳሁን መሪነት "የጥንዶች የመካንነት ህክምና የስኬት መጠን በአዲስ አበባ፣ ኢትዮጵያ" በሚል ርዕስ ስለሚደረገው የምርምር ፕሮጀክት ዝርዝር መረጃ ለማቅረብ ነው። እባክዎን ጥናቱን ለመቀላቀል ከመስማማትዎ በፊት በጥሞና ያዳምጡ/ ያንብቡ እንዲሁም ስለ ጥናቱ ማንኛውንም ጥያቄ ካሎት በነፃነት ይጠይቁ። ጥናቱን ከተቀላቀሉ በኋላም በማንኛውም ጊዜ ጥያቄዎችን መጠየቅ ይችላሉ።

የጥናቱ ዓላማ፡-

ይህ ጥናት በመካንነት ሕክምና ላይ ያለውን የሕክምና የስኬት መጠን ለማየት፣የመካንነት ሕክምናዎች ስኬታማ የሚሆኑበትን ጊዜ ለመለካት እና የወሊድ ሕክምና በወሰዱ ጥንዶች መካከል በሕክምናው ስኬት ላይ ተጽዕኖ የሚያሳድሩትን ነገሮች ለመለየት ያለመ ነው።

ሥነ-ምግባራዊ ጉዳዮች፡-

ስለ ጥናቱ ዝርዝር መረጃ ይሰጥዎታል በተጨማሪም ከመሳተፍዎ በፊት ፈቃደኝነትዎ ይጠየቃል። ተሳትፎዎ ሙሉ በሙሉ በፈቃደኝነት ላይ የተመሰረተ ነው፣ እናም ያለምንም ችግር ከጥናቱ መውጣት ይችላሉ እንዲሁም ማንነትዎ በሚስጥር ይጠበቃል።

የተሳትፎ ጥቅሞች እና ጉዳቶች

እርሶ በመሳተፎ፣ ስለ መካንነት ሕክምናዎች ስኬት ያለንን ግንዛቤ እና ለመካንነት ሕክምናዎች መሳካት የሚወስደውን የጊዜ መጠን ለማወቅ የሚያስችሉ ጠቃሚ መረጃዎችን ያበረክታሉ። ከእርስዎ ተሳትፎ ጋር የተያያዙ ምንም አይነት አደጋዎች እንዳሉ አንገምትም።

አድራሻ:

ስለ ጥናቱ ማንኛውም አይነት ጥያቄ ወይም ስጋት ካለዎት እባክዎን የሚከተሉትን በመጠቀም ዋና መርማሪዋን ሳሮን ካሳሁንን ያነጋግሩ።

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አሁን ወደ ጥያቄዎቹ መቀጠል እንችላለን?

አዎ _____ ቀጥል።

አይ _____አቁም።

የመረጃ ሰብሳቢው ስም፡- _____ የመረጃ ሰብሳቢው ፊርማ_____

ቀን፡ _____

ሰዓት_____

መጠይቅ

ተ.ቁ	ጥያቄዎች	ምላሽ	ወደ ተ.ቁ ...
1.	የ እርግዝናው ውጤት ምን ነበር?	1. በህይወት መወለድ → 2. የጽንስ መጨንገፍ ⟶ 3. ህይወቱ አልፎ መወለድ 4. በሂደት ላይ ያለ እርግዝና	ወደ ጥያቄ 2 እለፍ ወደ ጥያቄ 4 እለፍ
2.	የልደት ቀኑ መቼ ነበር?	––/––/–––– እ. ኤ. አ	
3.	የ ወሊድ ውጤት ምን ነበር?	1. ነጠላ ህጻን 2. መንታ 3. ሶስት ህጻናት 4. ሌላ––––––––––	
4.	ጽንሱ የጨነገፈው በየትኛው የ እርግዝና ወር ነበር?	1. በመጀመሪያዎቹ 3 ወራት 2. ከ 3 ወር በኋላ	