

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

REI SUBSPECIALITY UNIT

Prevalence, patterns and Treatment outcomes of abnormal semen parameters among infertile couples in Ethiopia: A Four-Year Retrospective study

By:

Dr. Nuredin Awel (MD, Final year REI fellow)

Advisors:

Dr. Mahlet Yigeremu (Assistant professor in OB-GYN, REI subspecialist)

Dr. Eyasu Mesfin (Associate professor in OB-GYN, REI subspecialist)

A Thesis submitted to the Department of Obstetrics and Gynecology, College of Health Sciences, Addis Ababa University in partial fulfillment of the requirements for the subspecialty in reproductive endocrinology and infertility.

December, 2025

Addis Ababa, Ethiopia

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF OBSTETRIC AND GYNECOLOGY

REI SUBSPECIALITY UNIT

Principal investigator	Dr. Nuredin Awel
Advisors	Advisors: - Dr. Mahlet Yigeremu (Associate professor in OB-GYN, REI subspecialist) Dr. Eyasu Mesfin (Associate professor in OB-GYN, REI subspecialist)
Title of research	Prevalence, patterns and Treatment outcomes of abnormal semen parameters among infertile couples in Ethiopia, A retrospective study
Duration of research	Two months
Study setting	September-October, 2025
Total cost of project	**106,150Birr**
Address	Dr. Nuredin Awel Phone number +251911393614

Acknowledgement

I would like to express my deepest heartfelt thanks to all those who contributed to the completion of this thesis. First of all, my sincere appreciation goes to my academic advisors, Dr. Mahlet Yigeremu and Dr. Eyasu Mesfin, whose insightful feedback, and constant encouragement were instrumental throughout every stage of this research. Their commitment to scientific rigor and mentorship has shaped both this work and my growth as a researcher.

I am equally indebted to the faculty and staff of the Department of Obstetrics and Gynecology at AAU college of health Sciences for allowing me to do this research thesis. Special gratitude to the participating private infertility centers in Addis Ababa, namely Al-Hikmah fertility and IVF center and Ethio fertility and IVF center, who provided access to patient records and facilitated data collection for this study. Their assistance was indispensable to the completion of this research, their cooperation in granting access to clinical records, laboratory data, and treatment information made this study possible. I am profoundly thankful to the clinicians working there specially Dr. Ibrahim Saleh and Dr Hassen Hussein, embryologists, and administrative personnel who offered invaluable technical support, and logistical assistance.

My gratitude also goes to my colleagues and fellow postgraduate students, whose constructive discussions, shared experiences, and moral support enriched the academic journey. I am particularly grateful to those who participated in data collection, database organization, and interpretation of laboratory findings.

I owe special appreciation to my family for their unconditional support, patience, and constant motivation. Their belief in my abilities sustained me through the most challenging moments of this journey. I also thank my friends, who provided balance, encouragement, and understanding throughout the research and writing process.

Last but not least, I acknowledge with sincere gratitude all the couples whose anonymized clinical data formed the foundation of this study. Their experiences and struggles with infertility are a powerful reminder of the importance of advancing reproductive medicine technology.

To all who contributed in ways large and small—thank you. Nuredin Awel Mohammed

Table of Contents

Declaration ..... **Error! Bookmark not defined.**

Acknowledgement 3

List of tables 6

List of Figures 7

List of Annex 8

List of Acronyms and Abbreviations 9

ABSTRACT 11

1. INTRODUCTION 13

1.1. Background 13

1.2. Statement of the Problem 16

1.3. Significance of the Study 18

2. LITERATURE REVIEW 19

2.1. Global and Regional Burden of Infertility 19

2.2. Prevalence of Abnormal Semen Parameters 19

2.8 Conceptual Framework ..... **Error! Bookmark not defined.**

3. OBJECTIVE 24

3.1. General objective: 24

3.2. Specific objectives: 24

4. METHODS AND MATERIALS 25

4.1. Study Setting and Period 25

4.3. Population 27

4.3.1. Source Population 27

4.3.2. Study Population 27

4.4. Eligibility Criteria 27

4.4.1. Inclusion Criteria 27

4.4.2. Exclusion Criteria 28

4.5. Sample Size Determination 28

4.6. Sampling Procedure 30
4.7. Study Variables 34
4.7.1. Dependent Variable 34
4.7.2. Independent Variables 34
4.8. Data Collection Instrument 35
4.9. Data Quality Assurance 36
4.10. Data Collection Procedure 37
4.11. Data Management, Analysis and Interpretation 39
4.12. Ethical Considerations 40
4.13. Operational Definitions 41
4.14. Dissemination of Results 44
5. RESULT 45
5.1 Socio-demographic, Lifestyle Factors and clinical information of study participants 45
5.6 . Treatment-Related Factors of the infertile couple with Treatment Distribution 57
5.7. Fertility Treatment Outcomes of infertile couple after first cycle IUI or ICSI 60
5.7.1 IUI Clinical Pregnancy Rate 60
5.9 Comparison Between Semen Abnormality and Clinical Characteristics 66
5.11 Clinical pregnancy rate 72
5.12 Determinants of clinical pregnancy 74
6. DISCUSSION 78
7. Strength and limitation of the study 87
8. CONCLUSION AND RECOMMENDATION 89
9. REFERENCES 92
ANNEXS 99
Annex I: Data abstraction form 99

List of tables

Table 1: Sociodemographic, lifestyle factors and clinical information among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 2: Reproductive history among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 3: Comparison between specific semen abnormality patterns across age and year of treatment among male partners of couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 3: Treatment related factors among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 4: Treatment related factors among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 4: Fertility treatment outcomes among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 5: Fertility treatment outcomes among couples who underwent First cycle IUI treatment in Ethiopia between July 2021 and June 2025 (n = 685)

Table 6: Fertility treatment outcomes among couples who underwent First Cycle ICSI treatment in Ethiopia between July 2021 and June 2025 (n = 557)

Table 7: Comparison between specific semen abnormality and clinical characteristics among male partners of couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 8: Determinants of clinical pregnancy among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

List of Figures

Figure 1: This study is anchored in a conceptual framework adapted from WHO (2021) and ASRM (2022), contextualized to the Ethiopian setting.

Figure 2: General description of collection of study participants` semen analysis classification with its treatment outcome from selected fertility centers between July 2021 and June 2025(n=1242)

Figure 3: Prevalence of abnormal semen pattern, sperm concentration, sperm motility, and sperm morphology using WHO 2021 classification in male partners of couples receiving infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Figure 4: Fertility treatment outcomes per treatment type among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Figure 5: Semen abnormality patterns per age group in male partners of couples receiving infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Figure 6: CPR-among couples receiving fertility treatment per semen volume, count and morphology status in Ethiopia between July 2021 and June 2025 (n = 1242)

Figure 7: CPR-among couples receiving fertility treatment per semen concentration and sperm motility status in Ethiopia between July 2021 and June 2025 (n = 1242)

Figure 8: Clinical pregnancy rate among couples receiving infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

List of Annex

ANNEX I: Data abstraction form

ANNEX II: Waiver of Consent Request

List of Acronyms and Abbreviations

Acronym	Full Form
AAU	Addis Ababa University
AFC	Antral Follicle Count
AMH	Anti-Müllerian Hormone
AOR	Adjusted Odds Ratio
ART	Assisted Reproductive Technology
ASRM	American Society for Reproductive Medicine
BMI	Body Mass Index
CI	Confidence Interval
COR	Crude Odds Ratio
DFI	DNA Fragmentation Index
DOR	Diminished Ovarian Reserve
DRPC	Departmental Research and Publication Committee
EDHS	Ethiopia Demographic and Health Survey
ET	Endometrial Thickness
FET	Frozen Embryo Transfer
FSH	Follicle-Stimulating Hormone
HCG	Human Chorionic Gonadotropin
ICSI	Intracytoplasmic Sperm Injection

IQR	Interquartile Range
IRB	Institutional Review Board
IUI	Intrauterine Insemination
IVF	In Vitro Fertilization
LH	Luteinizing Hormone
MII	Metaphase II
OAT	Oligo-Astheno-Teratozoospermia
PCOS	Polycystic Ovary Syndrome
PID	Pelvic Inflammatory Disease
POF	Premature Ovarian Failure
REI	Reproductive Endocrinology and Infertility
SD	Standard Deviation
SPHMMC	St. Paul's Hospital Millennium Medical College
TESE	Testicular Sperm Extraction
TMSC	Total Motile Sperm Count
TVS	Transvaginal Ultrasound
WHO	World Health Organization

ABSTRACT

Background: Infertility is a substantial public health burden in sub-Saharan Africa, yet evidence on assisted reproductive technology (ART) outcomes, particularly those related to male factor infertility, remains limited in Ethiopia. Semen analysis is a cornerstone to male fertility assessment; however, its prognostic significance for treatment success with intrauterine insemination (IUI) or intracytoplasmic sperm injection (ICSI) in low-resource settings is not well established. Despite expanding access to ART, data on the prevalence, patterns, and clinical relevance of abnormal semen parameters in Ethiopia are scarce. This study provides the first large-scale analysis of semen profiles and their association with ART outcomes among infertile couples in Ethiopia.

Objective: This study aimed at describing the prevalence and patterns of abnormal semen parameters and determining their association with fertility treatment outcomes between IUI and ICSI among infertile couples undergoing first-cycle ART at two private fertility centers in Addis Ababa, Ethiopia. between July 2021 and June 2025.

Methods: A four-year retrospective cross-sectional study was conducted among 1,242 consecutive infertile couples who underwent their first ART cycle (IUI or ICSI) between July 2021 and June 2025. Data were extracted from semen analysis records and treatment outcome registries, with semen analysis standardized per WHO 2021 criteria. The primary outcome was clinical pregnancy. Data were analyzed using SPSS version 26. Descriptive statistics were used to assess prevalence and patterns of semen abnormalities. Associations between semen parameters, reproductive characteristics, and clinical pregnancy were evaluated using chi-square tests and multivariable binary logistic regression. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported, with statistical significance set at $p < 0.05$.

Results: The mean age of male partners was 40.07 ± 7.78 years, while female partners had a mean age of 34.43 ± 11.69 years. Primary infertility accounted for 64.1% of couples where as Secondary infertility comprised 35.9%. Abnormal semen parameters were highly prevalent, observed in 55.6% (691/1242) of couples with a clinical pregnancy rate of (n=93, 13.5%). The most common isolated abnormalities were suboptimal motility (n=404, 32.5%), suboptimal count (n=347, 27.9%), and atypical morphology (n=221, 17.8%). Azoospermia (0 sperm/mL

accounted for n=12, with a prevalence of 1.0% of all men. During the study period treatment distribution was, 685 couples (55.2%) underwent IUI and 557 (44.8%) underwent IVF/ICSI, with corresponding clinical pregnancy rates of 7.7% and 19.0% respectively, yielding an overall clinical pregnancy rate of 12.8% (95% CI: 11.0–14.7%). In multivariable analysis, after adjustment for covariates, abnormal semen parameters were not independently predictive of clinical pregnancy. However, female age ≥35 years was associated with a 56% reduction in the odds of pregnancy compared to age <30 (AOR = 0.44, 95% CI: 0.27–0.74, p = 0.002). IVF/ICSI treatment conferred 3.65 times higher odds of success than IUI (AOR = 3.65, 95% CI: 2.31–5.78, p < 0.001).

Conclusion: More than half of infertile men presenting to private fertility centers in Ethiopia have at least one abnormal semen parameter. However, clinical pregnancy outcomes were primarily influenced by female age and treatment modality rather than semen abnormalities per se. The findings from this study suggest that semen analysis categories alone have limited prognostic role for predicting ART success in this setting.

Recommendation: Rather than depending just on semen parameter classifications, clinical counseling and treatment selection for IUI or ICSI should take a holistic, couple-centered approach that gives priority to female age and the overall clinical context. Prospective research is necessary to improve evidence-based classification of infertile couples receiving ART and to better understand the prognostic role of semen abnormalities in ART outcomes.

Keywords: infertility, IUI, ICSI clinical pregnancy, abnormal semen parameters, assisted reproductive technologies, Ethiopia

1. INTRODUCTION

1.1. Background

Infertility is widely known for its major public health and social impact globally posing a significant reproductive health challenge affecting couples socially, psychologically as well as medically (1). It is clinically defined as the inability to achieve pregnancy after at least twelve months of regular, unprotected intercourse for a woman below the age of 35 years, where as it is defined as inability to conceive after six months of regular and unprotected sexual intercourse for women above the age of 35 years (2). Despite many technological advances and diagnostic and therapeutic achievements in the field, the social and economic burden from infertility is still a high with an estimated 60-80 million couples experiencing it globally (3). Recent evidences also shows that there is a progressive decline in human fertility potential over the last several decades, both in low-income and high-income regions of the world, but the magnitude of the disease is huge and greatest in developing countries like Ethiopia (4-6). Most countries in Africa report disproportionately higher infertility rates, with estimates ranging between 20% and 35%, substantially exceeding those reported in the developed world such as; Europe and North America (7,8). Evidence from Ethiopia also indicates that there is an increasing trend in infertility burden, though systematic national data remain sparse (9).

Although infertility can come from either partner individually or in a combined factor form, male-related etiologies contribute substantially these days (3). It is a well-established fact that semen parameters including motility, morphology and sperm concentration, are critical for assessing the fertilizing capacity of spermatozoa (10). Men presenting with infertility frequently show identifiable abnormalities in one or more of these parameters in isolation or in combination (11,12). Abnormalities in semen parameters including impaired motility, reduced sperm concentration, and atypical morphology represent common mechanisms underlying male infertility (13,14). Semen analysis remains fundamental to male fertility evaluation as a result of its cost effectiveness, wide accessibility and diagnostically semen analysis is easily informative of the integrity of the male reproductive function (10,15-18). Semen analysis provides essential insights into sperm production, maturation, and functional competence. Studies indicate that

approximately one-quarter of infertility cases are primarily attributable to male factors, and up to 50.0% involve some contribution from male partner (19). The higher prevalence of semen abnormalities reported in various regions of Africa suggests the importance of male evaluation in day-to-day infertility care from the very first visit and initial consultation day (7,8).

Multiple conditions may contribute to impaired semen quality, including hormonal disturbances, testicular dysfunction, lifestyle and environmental exposures, infections, and metabolic or genetic abnormalities (20,21). Although several medical and surgical interventions such as antioxidants, ovulation-inducing agents, or varicocele repair have been attempted to improve sperm quality, their clear impact on actual pregnancy outcomes remains inconsistent (22-24). Consequently, assisted reproductive technologies (ART) such as intrauterine insemination (IUI), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI) play a key role in the management of moderate to severe male-factor infertility.

The assessment of male fertility with seminal fluid analysis has undergone a significant paradigm shift based on the 2021 WHO semen analysis guidelines. It has moved away from a rigid classification system based on fixed numeric thresholds to clinically contextual, and couple-centered approach. This updated framework integrates semen parameters such as total motile sperm count (TMSC), progressive motility, concentration, and morphology, and with key clinical variables including female age, ovarian reserve, and infertility duration. The primary aim is to guide individualized management and optimizing the selection of ART treatment modality type, thereby improving prognostication and avoiding unnecessary escalation to more invasive and costly treatments. (15).

Within this integrated model, treatment pathways are stratified according to the severity of semen abnormalities and the broader clinical context. For mild-to-moderate male factor infertility, IUI is considered reasonable when post-wash TMSC is ≥5–10 million. Conventional in vitro fertilization (IVF) is deemed appropriate for cases where semen quality is sufficient for natural fertilization in vitro, typically indicated by moderate defects. Conversely, ICSI is recommended for severe abnormalities such as TMSC <1 million, severe oligozoospermia, or

azoospermia as well as for previous IVF fertilization failure or high sperm DNA fragmentation. This refined, evidence-based stratification by WHO supports more precise and effective clinical decision-making in the management of male infertility in day-to-day clinical practice (15). Given its accessibility and diagnostic value, semen analysis plays a key role in identifying underlying possible causes of male factor infertility and guiding appropriate treatment strategies (25). Timely assessment of semen parameters at initial visit of infertile couples facilitates early intervention, improving the likelihood of achieving conception.

In Ethiopia, infertility in general and male infertility in particular is becoming more commoner than before with a significant social and public health implications. Although ART services are expanding, as a result of limited local data, the fertility services provided to the couple rely mainly on international protocols that might fully align with the country`s clinical realities in many ways (26). Understanding the prevalence and characteristics of semen abnormalities within the Ethiopian context is hence very fundamental for improving male factor infertility care, reinforcing diagnostic strategies, and developing evidence-based treatment pathways at individual couple level.

1.2. Statement of the Problem

The primary test for assessing male reproductive function is semen analysis and its accurate evaluation and interpretation has been standardized the WHO Laboratory Manual since 1980. However, semen analysis diagnostic and prognostic value is limited by considerable biological variability and multiple confounding factors such as testicular volume, endocrine function, abstinence duration, lifestyle and environmental exposures (27-30). The 2021 WHO manual introduced substantial conceptual and methodological changes with a more standardized and clinically contextualized approach shifting semen evaluation from rigid numerical thresholds and diagnostic classification toward a prognostic clinical tool, couple-centered interpretation that guides individualized management and ART decision-making (15,26,31).

However, in low-resource settings like Ethiopia major knowledge gap persists regarding the current real-world prevalence and patterns of abnormal semen parameters which are out side of the WHO2021 reference limits despite these updates.

However, despite these updates, major knowledge gaps persist regarding the current real-world prevalence and patterns of abnormal semen parameters which are outside of the WHO 2021 reference limits, particularly in low-resource settings like Ethiopia. While severe abnormalities such as azoospermia clearly indicate the need for advanced ART, especially ICSI (32-34), the optimal treatment pathways and expected treatment outcomes for men with mild-to-moderate or combined defects in concentration, motility, and morphology remain poorly defined.

Currently there is limited data on semen abnormality patterns within Ethiopian population and insufficient local evidence linking specific semen abnormalities with ART success probabilities. Furthermore, lack of locally validated thresholds for choosing between IUI and IVF/ ICSI and also heterogeneity in clinical practice among fertility centers and professionals in the field as a result of absence of national guidelines. Additionally, there is limited empirical evidence on how the updated WHO 2021 criteria translate into clinical outcomes for couples undergoing IUI or ICSI in routine clinical practice.

This study was therefore designed to fill the critical evidence gap by evaluating the prevalence and patterns of abnormal semen parameters in a large cohort of infertile Ethiopian couples, while

simultaneously assessing treatment outcomes for IUI and IVF/ICSI using the updated WHO 2021 framework on semen analysis. The results are intended to guide clinicians in selecting suitable treatment pathways for male-factor infertility at couple level within the Ethiopian healthcare context.

1.3. Significance of the Study

The goal of this research is to produce clinically useful and scientifically sound data about the frequency, trends, and reproductive consequences of aberrant semen parameters in Ethiopian infertile couples. It will produce high-quality, locally relevant evidence on male infertility, which is essential for improving Ethiopia's reproductive health services. This study probably offers pertinent clinical information that can enhance the diagnostic precision, clinical assessment and treatment of men who present with infertility by identifying the common types and distribution of semen abnormalities. Furthermore, connecting semen characteristics to actual treatment results sheds light on the relative use of IUI versus ICSI for male -factor infertile couples as well as the efficacy of current management techniques

The outcome will aid in the creation of tailored infertility care recommendations that are relevant to Ethiopia's clinical setting. These include setting more suitable ART referral standards, making the most of the laboratory and clinical tools at hand, and giving couples more precise expectations about the outcome of their treatment. From a broader public health standpoint, the study offers actual first-hand information that can guide national planning for the extension of reproductive health services, policy decisions, and resource allocation. The study offers empirical data that can guide national planning for the extension of reproductive health services, budget allocation, and policy decisions from a wider public health standpoint.

The results of this study will also provide a foundation for future investigations into the genetic, environmental, behavioral, and hormonal factors that affect male fertility in Ethiopia. In the end, the study improves pregnancy outcomes for infertile couples seeking reproductive help nationwide and increases equitable access to quality and economical infertility care.

2. LITERATURE REVIEW

2.1. Global and Regional Burden of Infertility

A major global public health concern, infertility affects many couples of reproductive age and has serious psychological, social, and financial repercussions (1,3,35). Due to its rising incidence and impact on family formation, particularly in low- and middle-income nations, infertility has drawn more attention in recent decades. Both sexes are affected by infertility, but male factor infertility has emerged as a major and often disregarded issue, either alone or in combination with female factors (20,36).

Infertility has significant societal ramifications in Sub-Saharan Africa, where the stigma associated with involuntary childlessness is heightened by cultural norms surrounding marriage and childbearing. Male reproductive dysfunction, either alone or in conjunction with female factors, accounts for a significant fraction of infertility cases throughout the region, despite the frequent emphasis on female-related causes. Delays in seeking medical attention, restricted access to fertility services, and a high rate of untreated reproductive tract infections all contribute to the burden (30,37).

2.2. Prevalence of Abnormal Semen Parameters

Male infertility is often evaluated by semen analysis, which remains the cornerstone of male reproductive examination (15). aberrant semen characteristics, including decreased sperm concentration, impaired motility, aberrant morphology, and decreased vitality, are frequently observed in infertile men worldwide (36). Male infertility has significantly increased over the past few decades, according to global analyses, with Sub-Saharan Africa reporting a particularly high burden (20,36).

According to WHO estimates, male factor infertility, either as a primary or combined cause, accounts for up to half of cases of infertility (15). According to pooled estimates, male factors account for over one-fifth of cases of infertility in African settings, while combined male and female causes account for an additional portion (37). Studies conducted in Ethiopia consistently

show that infertile men have a high prevalence of abnormal semen parameters; in several institutional studies, abnormalities were found in over half of the evaluated samples (38–41).

2.3. Patterns and Distribution of Abnormal Semen Parameters

The classification of anomalies in semen is guided by the World Health Organization's 2021 (6th edition) semen analysis manual, which provides reference values for semen volume, sperm concentration, total sperm count, motility, morphology, and vitality. Deviations from these characteristics are used to diagnose oligozoospermia, asthenozoospermia, teratozoospermia, necrozoospermia, azoospermia, and combination abnormalities (15).

Reduced sperm concentration and poor motility are the most often observed abnormalities among infertile men in different geographic regions (37, 38, 40, 42). The distribution of semen abnormalities varies greatly, according to studies done in Ethiopia; some centers describe asthenozoospermia as the most common abnormality, while others identify azoospermia or mixed abnormalities as the most common patterns (39,43,44). These differences most likely reflect differences in referral patterns, healthcare availability, environmental exposures, and lifestyle choices (20, 30).

2.4. Determinants of Abnormal Semen Parameters

A complex interplay of hormonal, metabolic, environmental, infectious, and lifestyle factors affects the quality of semen (20,45,46). Impaired spermatogenesis and aberrant semen profiles are closely linked to hormonal disorders, such as changed levels of gonadotropin and testosterone (45,46). Reduced sperm concentration and motility have also been associated with metabolic factors, including abnormal body mass index and long-term medical conditions (21,47).

Globally, environmental exposures, such as endocrine-disrupting chemicals and occupational toxins, are increasingly linked to declining semen quality (20). Studies conducted worldwide and in Ethiopia have repeatedly linked lifestyle choices like drinking alcohol, smoking cigarettes, and chewing khat to lower semen parameters (38,40,41,44). Through oxidative stress and compromised spermatogenesis, infections and inflammatory conditions of the male reproductive tract also contribute to sperm dysfunction (30).

2.5. Impact of Abnormal Semen Parameters on Fertility Treatment Outcomes

When choosing an infertility treatment and forecasting the results of assisted reproduction, semen quality is crucial. Sperm motility and total motile sperm count are important factors in determining the success of intrauterine insemination, which is frequently used for couples with mild male factor infertility. While severe semen abnormalities are typically linked to low success rates, reduced motility and a low total motile sperm count are consistently linked to worse IUI outcomes (48–50).

Treatment options for male factor infertility couples have been greatly enhanced by intracytoplasmic sperm injection and in vitro fertilization. In particular, ICSI circumvents natural selection barriers and permits fertilization even when there are severe abnormalities in the semen. However, there is still conflicting data about how well traditional semen parameters predict the results of IVF and ICSI. Basic semen parameters may not have much of an impact on pregnancy outcomes once viable sperm are available, especially in frozen embryo transfer cycles, according to some studies that report associations with fertilization and embryo development (48,51,52).

Recent research suggests that factors related to the embryo, particularly blastocyst morphology and inner cell mass quality, may be more important predictors of early pregnancy and implantation than traditional semen parameters or male age (52,53). These results imply that uterine receptivity and embryo quality, rather than just semen characteristics, are increasingly important for ART success.

2.6. Evidence from Ethiopia and Rationale for the Study

There is still a dearth of published Ethiopian data on male infertility and anomalies in semen. Studies that are currently available show that infertile men, especially in western and urban referral settings, significantly deviate from WHO reference values for sperm concentration, motility, morphology, and vitality (39,41,44). However, comparability with current international standards is limited because the majority of studies are single-center and were conducted before the WHO 2021 semen analysis criteria were adopted (15).

Large-scale, methodologically sound studies that integrate semen analysis with treatment outcomes are obviously needed, given Ethiopia's growing use of assisted reproductive technologies and the lack of national guidelines for infertility treatment. This study fills a significant national evidence gap by methodically assessing the prevalence, patterns, and treatment outcomes of abnormal semen parameters across IUI and IVF/ICSI modalities using updated WHO criteria.

2.7. Summary

According to the literature, abnormal semen parameters are very common among infertile men, and male infertility accounts for a significant portion of both global and regional infertility (20,36,37). The type and severity of these abnormalities vary significantly among populations and have a multifactorial origin (39, 40, 44). The prognostic value of semen analysis for assisted reproductive outcomes, especially in the context of ICSI, is still up for debate, despite the fact that it is still crucial for diagnosis and treatment selection (51–53). By offering thorough, up-to-date, Ethiopia-specific data on semen abnormalities and the results of fertility treatments, this study expands on previous research.

2.8 Conceptual Framework

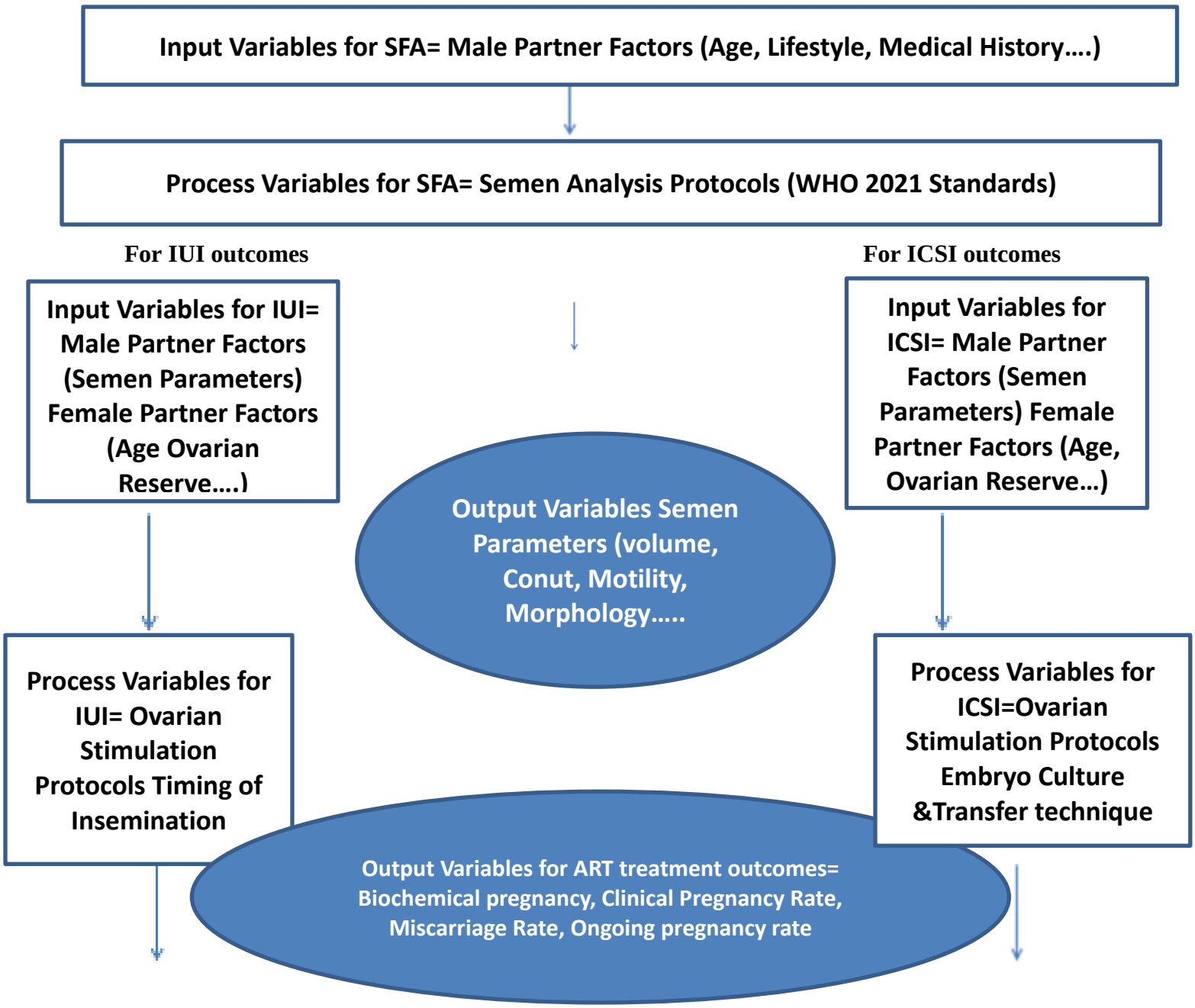


Figure 2: This study is based on a conceptual framework that was contextualized to the Ethiopian context and modified from the WHO (2021) semen analysis standards (15) and ASRM (2022), (26).

3. OBJECTIVE

3.1. General objective:

- To assess the prevalence and patterns of abnormal semen parameters and to determine their association with fertility treatment outcomes between IUI and ICSI among infertile couples treated with first-cycle ART at selected two private centers in Ethiopia between July 2021 and June 2025.

3.2. Specific objectives:

- To determine the prevalence of abnormal semen parameters among infertile couples using the updated WHO 2021 criteria (15).
- To describe the types and distribution patterns of abnormal semen parameters as per the updated WHO 2021 criteria.
- To evaluate the fertility treatment options utilized for the infertile couples with abnormal semen parameters compared to those normal semen parameters, including IUI and IVF/ICSI.
- To assess the treatment outcomes of infertile couples with various types of abnormal semen parameters, including fertilization rate, biochemical pregnancy, clinical pregnancy, and ongoing pregnancy rate.

4. METHODS AND MATERIALS

4.1. Study Setting and Period

This study was conducted in Addis Ababa, the capital city of Ethiopia, the country's principal hub for infertility care and assisted reproductive technology (ART) services. Ethiopia currently has a limited number of licensed ART centers, with Addis Ababa hosting the majority of facilities equipped to perform IUI, IVF, and ICSI. According to information obtained from the Ethiopian Federal Ministry of Health, there are six licensed and functional fertility centers in Ethiopia, all located in Addis Ababa except one, Ado IVF Center, located in Tigray region. Of the five Centers in Addis Ababa, one is a public fertility center, St. Paul's Hospital Millennium Medical College (SPHMMC) IVF Center and the other four are private centers which includes Al Hikmah Fertility Center, New Leaf Fertility Center, Ethio-Fertility IVF Center and the recently established Ethio-Tebib Hospital, which is launched only a year ago.

This study was conducted in two major private fertility centers in Addis Ababa, Ethiopia. Both centers serve as high-volume referral facilities offering comprehensive infertility evaluation and treatment services, including semen analysis, ovulation induction, IUI, IVF, and ICSI. They receive clients from Addis Ababa as well as from different parts of the country, making them representative of Ethiopia's urban infertility care landscape. The two selected private fertility centers are namely: AL-HIKMAH Fertility Clinic and ETHIO-FERTILITY Clinic. They carry out all diagnostic laboratory tests, including semen analyses, and also ART procedures according to a standardized clinical and laboratory protocols adopted from WHO.

AL-HIKMAH Fertility Clinic is one of the country's Pioneered most reputable IVF centers, offering a wide range of assisted reproductive technologies including IVF, ICSI, IUI for the last ten years. The center also provides a range of diagnostic evaluations such as hormone testing for both partners, ultrasonography, and semen analysis staffed by experienced and senior fertility sub-specialists and embryologists. It is also known for its transparency and affordable price.

The second fertility center selected in this study was Ethio fertility and IVF Center, which is a private fertility center that has been operating as of 2021 G.C. as one of the private IVF centers in the country. It provides comprehensive male and female infertility treatment, including assisted reproductive technology, namely IVF, ICSI, and IUI; minimally invasive surgeries like laparoscopy and hysteroscopy; and general and sub-specialty level consultations in reproductive health with good public and government reputation for its affordability and quality of care for the last five years.

Both centers adhere to WHO laboratory standards for conducting semen analysis for the men partner (15,59) and follow internationally acceptable and evidence-based ART protocols using ASRM and ESHRE recommendations (26). The study period window was four-year beginning from July 2021 up to June 2025 inclusive, allowing adequate follow-up time for assessing clinical pregnancy rate outcomes in couples who underwent their first-cycle ART. Data collection was collected over a period of two-months, from September-October 2025, ensuring a retrospective design with complete cycle documentation using kobo toolbox from a total of 1242 first attempt ART treatment cycles.

4.2. Study Design

A retrospective cross-sectional design was used to review clinical records of infertile couples evaluated and treated with first-cycle IUI or ICSI between July 2021 and June 2025. This design was chosen because it enables assessment of semen characteristics and treatment outcomes over multiple years using routine clinical data from a large patient population at low cost.

An institution-based retrospective study design was employed among couples who underwent infertility treatment at the two fertility centers. The study included a comprehensive review of medical records both electronic and paper based, ART registries, and laboratory reports of infertile couples who underwent their first-cycle IUI or first-cycle ICSI fertility treatment **between July 2021 and June 2025 (n = 1242).**

The four-year window was strategically selected to ensure that, at the time of data collection, each included couples gave semen samples and received fertility treatment exactly after the last updated WHO 2021 recommendation guideline for semen analysis. Additionally, female partners

of each couple would have at least a minimum of three months of follow-up from the date of treatment initiation with IUI or ICSI. This duration was considered sufficient to observe the primary outcome, clinical pregnancy, which is typically confirmed within days to a few weeks of treatment initiation. Therefore, this follow-up period was deemed adequate for achieving the study objectives while ensuring data completeness and feasibility.

4.3. Population

4.3.1. Source Population

All infertile couples receiving diagnostic evaluation and/or ART at licensed fertility centers in Ethiopia during the defined study period. between July 2021 and June 2025.

4.3.2. Study Population

Infertile couples who underwent baseline semen analysis and subsequently received first fertility treatment (IUI or IVF/ICSI) at participating centers during the study period and within the three months prior to the start of data collection and who meet the eligibility criteria.
Each couple contributed only one treatment cycle to avoid clustering and reduce bias.

4.4. Eligibility Criteria

4.4.1. Inclusion Criteria

Participants were eligible for inclusion if they met the following conditions:

- Male partners of infertile couples with at least one documented semen analysis or who underwent testicular sperm extraction (TESE) at participating IVF centers during the study period.
- Couples undergoing their first IUI or ICSI treatment cycle within the study period, with a linked semen analysis performed within three months prior to the procedure.

- Treatment cycles with complete documentation of clinical evaluation, ovarian stimulation protocols, and laboratory procedures.
- Only the first laboratory evaluation of the semen analysis and first treatment cycle per each infertile couple were only included avoiding duplication, inter-cycle dependency, and minimizing selection bias.

4.4.2. Exclusion Criteria

The following cases were excluded from the study:

- Semen analyses performed within three months prior to data collection for which corresponding treatment outcomes could not be ascertained.
- Semen samples collected after initiation of treatment.
- Couples who were diagnosed with infertility after evaluation but did not proceed to the fertility treatment due to financial, medical, or social reasons.
- Semen samples processed outside the study facilities lacking complete raw data or adequate documentation of the laboratory methods used for semen analysis
- Repeat semen samples analyzed from the same patient during the study period; only the first analysis with full documentation was included.
- Semen samples for couples receiving conventional in vitro fertilization (IVF).
  These criteria for inclusion and exclusion ensured internal validity, minimize confounding, and maintain consistency with WHO and ASRM guidelines (15,26).

4.5. Sample Size Determination

Sample size determination for objective 1 & 2: prevalence estimation and description of patterns

The sample size was calculated using the single population proportion formula. Considering a z value of 1.96 for 95% confidence interval, 62.4% male factor infertility among infertile couples in a retrospective cross-sectional study SPHMMC IN 2022 in Addis Ababa (44) and 5% of margin of error.

$$n = \frac{Z_{\frac{\alpha}{2}}^{2} P (1 - P)}{d^{2}}$$

Where;

n = sample size

Zα/2 = critical value

95%CI= 1.96 (α = 0.05).

Proportion = 62.4% male factor infertility

margin of error= 5%

n=1.96 x 1.96 x 0.624(1-0.624)/0.05 x 0.05

n=361

The sample size was initially determined using the single population proportion formula, with the prevalence of abnormal semen parameters estimated at 62.4% from recent study, a 95% confidence level, and a 5% margin of error. This yielded a minimum of 361 participants. To account for a 20% rate of incomplete or missing data, the sample size was increased to 451.

Sample Size Considerations for Subgroup and Internal Comparisons

Although the primary objective of this cross-sectional analysis was prevalence estimation, internal comparisons across predefined subgroups were performed. Due to the retrospective nature the study design and therefore the use of all eligible records, formal subgroup-specific sample size recalculation was not undertaken. Sample size adequacy was rather assessed based on adequate or sufficient subgroup counts with minimum cell count requirements for bivariate analyses and events-per-variable criteria for multivariable regression. Subgroup and internal comparisons were performed within the cross-sectional analysis. Subgroup findings were interpreted cautiously as exploratory.

As the study was a retrospective chart review study using secondary data, we included all eligible participants whose documents were available, totaling (n=1,242) couples with complete semen analysis records for the final analysis to maximize statistical power and precision. The final sample size included in this study exceeded the minimum sample size requirement for each specific objective indicating that the study was more than adequately powered.

4.6. Sampling Procedure

A consecutive sampling with near census approach was used to enroll all eligible cases meeting the eligibility criteria who underwent first-cycle treatment during the defined study period at the selected private fertility centers in Addis Ababa. Ensuring maximal statistical power additionally eliminated sampling error. (**Figure 2)**

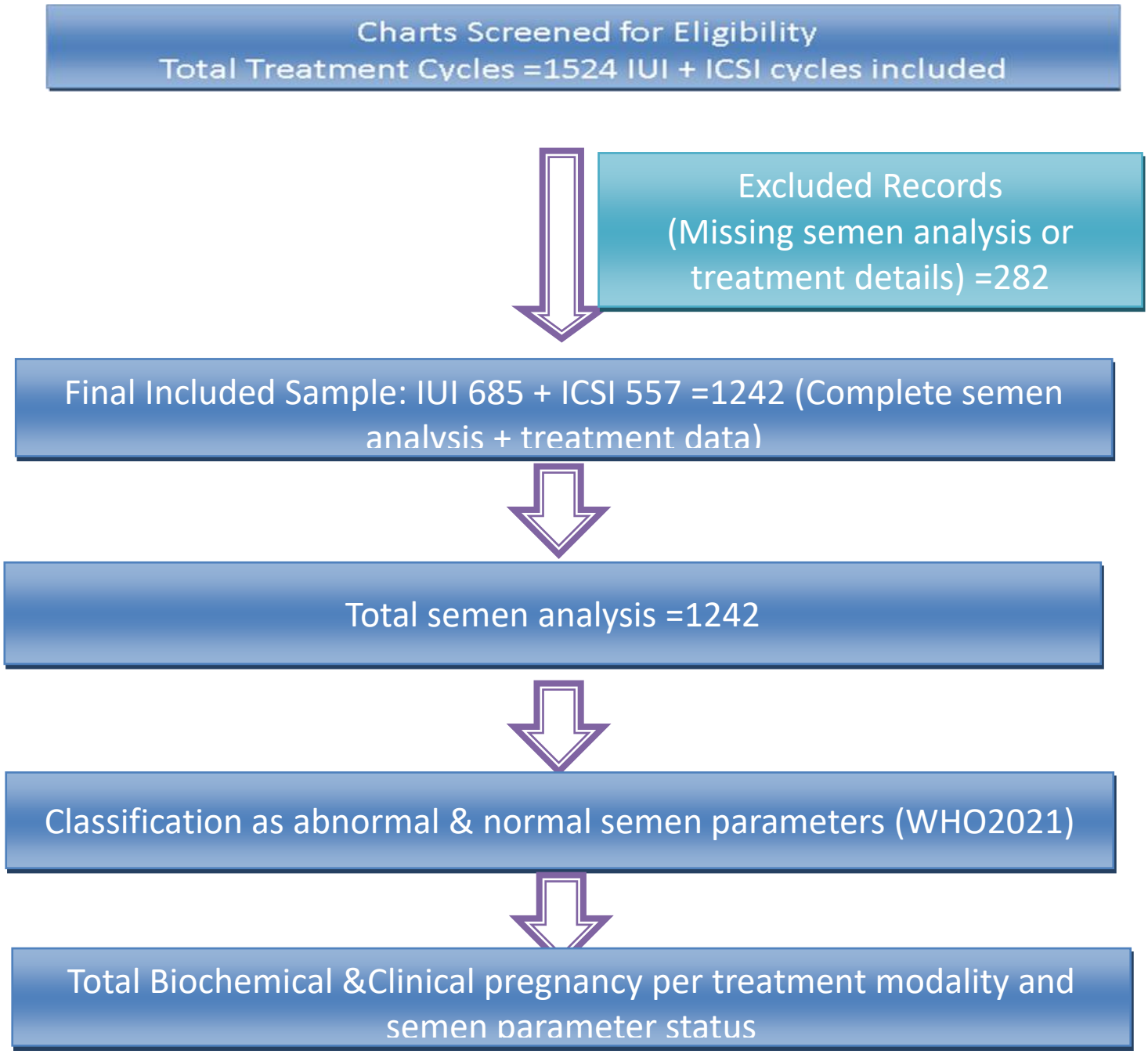


Figure 2: General description of collection of study participants` semen analysis classification with its treatment outcome from selected fertility centers between July 2021 and June 2025(n=1242)

Semen Collection and Laboratory Processing

In this study semen handling and preparation followed basic standard clinical practices applied routinely in Ethiopian fertility centers and were according to international recommendations for assisted reproductive technology. Semen samples were collected after clear instruction was given to the couple by masturbation, to provide ejaculated semen, after a period of abstinence from sexual activity for a period ranging from 2 to 7 days and collected in a wide mouthed sterile container. Collected semen samples were then allowed to liquefy at ambient laboratory temperature for approximately 30 minutes. In accordance with the WHO 2021 laboratory guidelines, initial semen evaluation was conducted including assessment of semen volume, sperm concentration, motility, and morphology (15,59).

Semen Processing for Intrauterine Insemination (IUI)

For intrauterine insemination cycles, semen samples were prepared using either density gradient centrifugation or the swim-up technique, depending on baseline semen characteristics and routine laboratory protocols. Density gradient centrifugation was most commonly employed, particularly in cases with abnormal semen parameters. Following liquefaction, semen was layered onto a two-step density gradient (40% and 80%) and centrifuged at 300–400 g for 15–20 minutes. Next, the pellet containing good number of motile spermatozoa will be recovered and washed with sperm preparation medium and centrifuged again to remove residual seminal plasma and contaminants. The final processed sample was again suspended in a volume of 0.3-0.5 ml before insemination to the female partner.

The swim-up method was also selectively utilized in men with normal semen parameters. After washing, culture medium will be gently layered over the semen pellet and incubated to allow upward migration of progressively motile sperm. The supernatant containing motile spermatozoa was aspirated and used for insemination. All inseminations were carried out within one hour of semen preparation in accordance with international guidelines. The total motile sperm count following preparation was documented for each IUI cycle and included in subsequent analyses (16).

Semen Processing for Intracytoplasmic Sperm Injection (ICSI)

In ICSI cycles using ejaculated sperm, semen samples were processed using density gradient centrifugation or simple washing techniques, depending on sperm concentration and motility. In cases of very low sperm count or markedly reduced motility, minimal processing was applied to avoid sperm loss. In treatment cycles involving ICSI, as fertilization involves direct injection of a single spermatozoon into the oocyte, emphasis was placed on sperm viability and morphology rather than total sperm count. Both motile sperm and immotile but viable sperm were considered suitable for microinjection in line with standard ART laboratory practices (26).

Processing of Testicular Sperm (TESE)

In selected cases of azoospermia or severe male factor infertility testicular sperm extraction was performed. Retrieved testicular tissue was immediately placed in pre-warmed sperm culture medium and transferred to the embryology unit. Disaggregation of seminiferous tubules was carried out mechanically using sterile fine scissors or needles to release spermatozoa. Enzymatic digestion was employed to improve sperm recovery in selected samples. The processed tissue suspension was centrifuged at low speed, and the resulting pellet was finally examined under an inverted microscope for the presence of viable sperm.

Motile spermatozoa were preferentially selected for ICSI. When spermatozoa were immotile, viability was assessed using mechanical tail stimulation or hypo-osmotic swelling testing. Based on availability of oocyte and clinical conditions, retrieved sperms were either used immediately or cryopreserved for possible future ICSI cycles as necessary (17).

Laboratory Quality Assurance

In both IVF centers, every semen handling procedure and preparation were carried out under strict controlled laboratory conditions: appropriate temperature was maintained, laboratory equipment's were routinely calibrated, aseptic technique strictly applied. These routines in the

laboratory were consistent with both national and international ART quality recommendations and standard operational guidelines in fertility center laboratories worldwide. All details of semen processing methods and post preparation sperm parameters were clearly documented in the patient medical chart and they were extracted for retrospective analysis for this study.

4.7. Study Variables

4.7.1. Dependent Variable

- Occurrence of abnormal semen parameters (based on WHO 2021 criteria).
- Patterns/types of semen abnormalities
- ART outcomes following IUI or ICSI (specifically Clinical Pregnancy)

4.7.2. Independent Variables

Sociodemographic and Lifestyle Factors

- Age of male partner
- Age of female partner
- Place of residence
- Treatment Clinic
- Duration of Marriage
- Female BMI
- Male Substance Use

Medical History

- Chronic Medical Illness (Female)
- Chronic Medical Illness (Male)
- History of Pelvic/Inguinal Surgery
- History of Varicocele

Reproductive and Diagnostic History

- Type of infertility
- Duration of infertility
- Previous Pregnancy Status

Treatment-Related Factors

- History of Previous Fertility Treatment
- Current Treatment Type
- IUI Indications
- IVF/ICSI Indications
- Cycle Type
- Stimulation Protocol
- Embryo Transfer Stage
- Number of Embryos Transferred

4.8. Data Collection Instrument

A structured, pretested data extraction form created especially for the retrospective review of patient clinical records was used to gather the data. International fertility guidelines, the WHO Laboratory Manual for the Examination and Processing of Human Semen (6th edition, 2021), and a thorough review of existing literature served as the foundation for the form's development. Key variables pertinent to the study, such as sociodemographic information, medical and reproductive history, semen analysis results, and treatment outcomes, were arranged in the data extraction form. To guarantee clarity and enable precise abstraction from patient records, every data field was carefully worded.

To guarantee clarity, content validity, and contextual appropriateness, the English-language tool was reviewed by subject matter experts, including academic advisors, public health specialists, and fertility subspecialists. In order for data collectors to accurately and consistently record information from charts, emphasis was placed on making sure that each variable is operationally defined. The form was pilot-tested on a limited number of eligible clinical records prior to full-

scale data collection in order to find and fix any ambiguities, inconsistencies, or interpretation challenges. As a result, changes were made to improve accuracy and usability.

Because of the nature of the study, the data collectors were clinical nurses and general practitioners with clinical experience and familiarity with medical terminology. This ensured that they could accurately interpret clinical records and accurately transcribe the necessary data into the extraction form. Understanding the data fields, interpreting clinical documentation, and upholding strict confidentiality throughout the abstraction process were all major topics of discussion during training sessions. This procedure guaranteed that the data collection instrument was both scientifically sound and efficient in gathering accurate and thorough data.

4.9. Data Quality Assurance

All data collectors and supervisors received three days of intensive training prior to the commencement of data collection, which covered the study's objectives, specific data abstraction procedures, ethical issues, and the significance of upholding strict confidentiality. In order to ensure accurate interpretation of clinical records and laboratory results, the data collection team was made up of general practitioners (GPs) and clinical nurses (CNs) who worked in the IVF lab and outpatient department (OPD) and had prior clinical experience. These CNs as data collectors and GPs as supervisors received additional training to improve their comprehension of confidentiality obligations in both clinical practice and research settings, as well as to match their chart review abilities with the particular variables needed for the study.

The assigned supervisors at each center conducted a daily on-site supervision and reviewed the completed kobo collect forms for consistency, accuracy and completeness. Discrepancies and missing information were identified and communicated immediately to the data collectors for timely correction based on the source document. Periodic random checks of the entered data were performed by the principal investigator to validate accuracy and ensure adherence to the protocol. All corrections were documented, and a final round of data quality review was carried out before data cleaning and analysis.

4.10. Data Collection Procedure

A structured, pretested data abstraction tool (developed in English) which consisted of all necessary variables, socio-demographic characteristics, clinical characteristics, semen analysis results, treatment procedures, and outcomes, was used to collect data from patient charts.

The tool was pretested on a small number of randomly selected eligible records, and necessary amendments were made to develop the final abstraction tool.

Data were collected by four BSc Nurses and two GPs as supervisors who received three days of intensive training on the data abstraction tool's handling, clinical record interpretation, and ethical considerations prior to the start of data collection.

The collected data were checked for consistency and completeness by the supervisors at both centers before being coded, entered, and analyzed.

Data was obtained retrospectively through structured chart reviews from the selected fertility centers. No patient contact or interview was conducted at any stage of the study.

Identification of eligible records

- Potential records were identified by reviewing the ART registry, laboratory logbooks, and medical chart databases maintained at each fertility center.
- The data collection team, consisting of two experienced clinical nurses and one GP as supervisor per center, was given a three-day training on the details of data collection procedure
- The data collecting team was working in collaboration with the center’s authorized medical records personnel and IVF lab staffs to ensure proper identification of records that meet the pre-defined inclusion and exclusion criteria.
- Each record was screened only on-site and was not removed from the facility.

Confidentiality and anonymization measures

- No personal identifiers (such as names, phone numbers, addresses, or medical record numbers) were entered into the kobo collect digital data collection tool.
- Each record was assigned a unique study code to link the extracted clinical data to the corresponding patient record during data cleaning.
- A temporary identifier–code list (linking study codes to patient identifiers) will be maintained only for operational purposes (e.g., to prevent duplicate entry of the same patient). this list was:
    - Stored separately from the study database.
    - Kept in a password-protected, encrypted file on an encrypted flash drive.
    - Accessible only to the principal investigator.
    - Permanently deleted after data entry and cleaning are completed, and any printed versions will be shredded.

Avoiding double counting

- Before entering a record into kobo collect, the study code was cross-checked against the temporary identifier–code list to ensure the same patient's data is not entered more than once.
- Only the first eligible treatment cycle for each patient within the study period was included for outcome analysis, unless otherwise specified in the protocol.

Data entry and storage

- Data were extracted directly from electronic and paper based clinical charts, laboratory reports, and art registries into kobo collect, which were configured with encryption, enabled and set to upload via secure (https) connections only.
- After successful upload to the secure server, data were immediately deleted from the collection device.
- The final anonymized dataset was stored in a password-protected computer and backed up on an encrypted drive accessible only to the principal investigator.

Institutional permission

- Prior to data collection, formal written permission was obtained from the administrative heads of each participating fertility center.

4.11. Data Management, Analysis and Interpretation

The collected data were coded, entered into Kobo Collect, cleaned using EpiData version 4.2.0, and subsequently exported to SPSS software version 26 for statistical analysis.

Clinical characteristics and baseline sociodemographic of the participants` were summarized using descriptive statistics. Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range [IQR]) and Categorical variables were expressed as frequencies and proportions (percentages) based on the distribution and nature of the data.

Treatment outcomes of male partners and their clinical characteristics were compared based on the semen abnormality severity pattern distribution using the Chi-square test, with statistical significance set at a p-value < 0.05. Fisher's exact test was used in cases where the assumptions of the Chi-square test were violated.

The association between independent variables including patterns of semen abnormalities and the primary outcome which is clinical pregnancy was examined using a binary logistic regression model. First univariate analysis was performed using a liberal significance level of $p < 0.25$ to screen and identify potentially relevant independent variables for inclusion in the final multivariable model.

Finally, to adjust for potential confounding, multivariable binary logistic regression was then performed using the screened variables with p value < 0.25 from the univariate test. The strength and direction of associations were expressed as adjusted odds ratios (AOR) with corresponding 95% confidence intervals (CI) and p-values. In the final model, independent variables with a p-value ≤ 0.05 were considered statistically significant predictors of clinical pregnancy.

The goodness-of-fit of the final logistic regression model was assessed using the Hosmer–Lemeshow test where p-value of >0.05 indicates adequate model for the data.

All analyses were conducted using the intention-to-treat principle. The denominator for pregnancy outcomes included all initiated IUI and ICSI cycles. Cycles with undocumented

pregnancy outcomes were retained in the analysis and conservatively classified as non-pregnant. Sensitivity analyses were performed using complete-case analysis and best-case assumptions to assess the robustness of the findings to missing outcome data.

4.12. Ethical Considerations

The study was conducted after receiving Ethical Clearance from the Departmental Research and Publication Committee (DRPC) of Addis Ababa University, College of Health Sciences).

A waiver of informed consent was formally requested and granted due to the retrospective nature of the chart review in our study design minimizing direct patient contact and intrusion. Formal written permissions were granted from the medical director of each IVF center on behalf of the study participants.

The privacy, confidentiality and anonymity of the participants were maintained throughout the study period. All electronic data were stored on a password-protected, encrypted drives, access to the collected clinical and non-clinical information regarding the study participants was limited to the principal investigator and authorized data collectors only.

Ethical Approval and Waiver of Consent

Given the retrospective design, obtaining individual informed consent is impracticable and may compromise patient confidentiality. Therefore, a waiver of informed consent was formally requested and granted on the grounds that: All procedures were completed prior to the study, contacting patients could be considered an invasion of privacy and could cause unnecessary anxiety and the study posed minimal risk to the individuals, because only anonymized, routinely collected clinical and sociodemographic data were reviewed for the study.

Confidentiality and Data Security Measures

Throughout the research process strong measures applied to protect patient privacy:

Anonymization at Point of Collection: Any personal identifiers like names addresses and phone numbers was not entered in the kobo collect form only relevant information to the study were abstracted.

Use of Unique Study Codes: Each record was assigned a unique study code.

Temporary Identifier–Code List: Where necessary to avoid duplicate entries, temporarily short list of patient identifiers linking to the study codes was used and maintained separately in a password-protected, encrypted file and their access was limited only to the principal investigator. This file was permanently deleted once data cleaning is complete.

Secure Storage of Physical Documents: If any physical notes containing identifiers are generated, they were stored in a locked cabinet accessible only to the principal investigator and were shredded immediately after use.

Secure Storage of Electronic Data: All electronic data were stored on a password-protected computer and backed up on an encrypted drive. Kobo Collect forms were had encryption enabled and upload only via secure (HTTPS) connections. Data were removed from collection devices immediately after successful upload to the secure server.

Restricted Access: Only the principal investigator and authorized data collectors had access to raw data during the collection phase. All analysis was performed on fully anonymized datasets.

Use of Data

all data were used exclusively for the purposes of this research. No identifiable information was shared with any third party. The findings were reported only in aggregated form, ensuring that no individual can be identified.

Institutional Permissions

Before initiating data collection, formal written permission was obtained from each participating fertility center.

4.13. Operational Definitions

- **Normal Semen Parameters:** Normal semen parameters are defined according to the World Health Organization (WHO) 2021, 6th Edition criteria:

Parameter	Reference Value (5th Percentile, 95% CI)
Semen Volume (mL)	≥ 1.4 (1.3–1.5)
Total Sperm Number (×10^6/ejaculate)	≥ 39 (35–40)
Sperm concentration ((×10^6/ejaculate)/ml	≥ 16M/ml
Total Motility (%)	≥ 42 (40–43)
Progressive Motility (%)	≥ 30 (29–31)
Vitality (%)	≥ 54 (50–56)
Morphologically Normal Forms (%)	≥ 4 (3.9–4.0)

- **Abnormal semen parameter:** Abnormality in semen analysis result in at least one of major sperm parameter namely sperm concentration, motility and morphology of male partner i.e. **any** one or more of the semen characteristics falling below WHO 2021 reference thresholds.
- **Older terminologies** were used interchangeably with the updated definitions for the purpose of comparison with other studies, understanding and communication only otherwise the updated definition discourages use of these terminologies
- **Oligozoospermia** for low count below the 5th percentile cutoff
- **Asthenozoospermia** for reduced motility and below the 5th percentile cutoff
- **Teratozoospermia** or atypical forms for morphology below the 5th percentile WHO 2021
- **TMSC:** Total number of progressively motile sperm in the ejaculate after processing**.**
- **TMSC Categories**: < 1 million Very Poor very low IUI success, <5 million (Poor), 5-10 million (Borderline), >10 million (Adequate) for IUI prognosis.
- **Primary infertility**- when a pregnancy has never been achieved by a person/couple.
- **Secondary infertility**- at least one prior pregnancy has been achieved a person/couple
- **Male-factor only**: clinically significant abnormal semen parameters and no clinically significant female infertility diagnosis.

- **Female-factor only**: clinically significant female infertility diagnosis (tubal disease, ovulatory disorder, endometriosis, diminished ovarian reserve, uterine anomaly) and normal semen parameters.
- **Mixed (combined) factor**: both a clinically meaningful male factor (abnormal semen per your chosen classification) and a clinically meaningful female factor.
- **Unexplained infertility:** standard workup normal for both partners with no clear cause.
- **Pregnancy Outcomes**
    - **Biochemical Pregnancy**: The presence of pregnancy confirmed by a positive serum β-HCG measurement above the laboratory's defined cutoff (≥ 25 Miu/mL) measured at approximately 12–14 days after IUI or embryo transfer.
    - **Clinical Pregnancy**: The presence or visualization of an intrauterine gestational sac on ultrasound (with or without fetal cardiac activity) typically achieved at ~5–7 weeks' gestation after embryo transfer or insemination.
    - **Ongoing Pregnancy**: A documented viable intrauterine pregnancy with fetal cardiac activity at or beyond 12 completed weeks of gestation.
- **Female Diagnostic Markers**
    - **Endometrial Thickness (ET)**: The measurement of the lining of the uterus.
        - Thin: ET ≤ 7 mm
        - Optimal: ET = 8 to 14 mm
        - Thick: ET > 14 mm
- **Antral Follicle Count (AFC)**: A measure of the number of follicles on the ovaries, determined using an ultrasound examination, providing insight into ovarian reserve.
    - Normal: AFC ≥ 5
    - Abnormal (Low): AFC < 5
- T**reatment year 2021:** defined as July 2021-June 2022,
- **Treatment year 2022:** defined as July 2022- June 2023
- **Treatment year 2023:** defined as July 2023-June 2024
- **Treatment year 2024:** defined as July 2024-June 2025

4.14. Dissemination of Results

Following data analysis and final write-up, the study results will be presented in a public defense at Addis Ababa University, Department of Obstetrics and Gynecology. Upon successful defense and incorporation of examiner feedback, the final report will be disseminated to key stakeholders, including the participating fertility centers, relevant policy-making bodies within the Ethiopian Ministry of Health, and the academic community through departmental presentations. Furthermore, a manuscript will be submitted for publication in a peer-reviewed journal to share the findings with the wider national and international scientific community.

5. RESULT

5.1 Socio-demographic, Lifestyle Factors and clinical information of study participants

A total of 1,242 infertile couples were included in the study who met the inclusion criteria. The majority of them of the couples 826(66.5%) resided in Addis Ababa, while the remaining participants were from outside the city 324(26.1%) or from outside of Ethiopia 92(7.4%).

Regarding age distribution, the male partners had a mean age of 40.1 ± 7.7 years, showing a relatively even spread across the age categories examined. The highest proportion of men fell into the 35–39 year 345(27.8%), followed closely by those aged ≥ 45 years 325(26.2%). Female partners had a mean age of 34.2 ± 5.9 years, and nearly half of the women 620(49.9%) were aged ≥ 35 years. All participants were married, with a median duration of marriage of 6 years (interquartile range [IQR]: 3–9 years).

A relatively higher proportion of male participants 129(10.4%) reported having at least one chronic medical condition compared to females, with 1,113 men (89.6%) reporting none. The most frequent chronic conditions among the 129 affected men were hypertension (n=52) and diabetes mellitus (n=43). Other reported conditions included other chronic illnesses (n=46), HIV (n=21), and Hepatitis (n=16). Less common conditions included cardiac disease (n=3), asthma (n=1), cholesterol disorder (n=1), epilepsy (n=1), impotence (n=1), renal/kidney surgery (n=1), and tuberculosis (n=1).

With respect to male substance use, the majority of men1232 (99.2%) reported no substance use. Only ten men (0.8%) reported using substances, which included alcohol use (n=4), cigarette smoking (n=6), and khat (chat) use (n=7).

Regarding surgical history relevant to male infertility, 114 (9.2%) of men reported previous pelvic or inguinal surgery. The prevalence of clinically diagnosed varicocele was very low, reported in only five men (0.4 %). (**Table 1)**

Table 1: Sociodemographic, lifestyle factors and clinical information among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025(n = 1242)

Variable	Category	Frequency	Percent
Address of couple	Addis Ababa	826	66.5
	Outside of A. A	324	26.1
	Outside of Ethiopia	92	7.4
Female Age (years)	< 30	281	22.6
	30-34	341	27.5
	≥ 35	620	49.9
Male Age (years)	< 35	296	23.8
	35-39	345	27.8
	40-44	276	22.2
	≥ 45	325	26.2
Male Substance Use	No	1232	99.2
	Yes	10	0.8
Chronic Medical Illness (male)	No	1113	89.6
	Yes	129	10.4
Pelvic / Inguinal Surgery	No	1128	90.8
	Yes	114	9.2
Varicocele (male)	No	1127	99.6
	Yes	5	0.4
Chronic Medical Illness (female partner)	No	1181	95.1
	Yes	61	4.9
Pelvic TB (female partner)	No	1229	99.0
	Yes	13	1.0

5.2 The reproductive characteristics of the female partner among infertile couples

Among the female participants, the majority (64.1%, n=796) presented with primary infertility, while 35.9 % (n=446) had secondary infertility. The overall median duration of infertility for the study population was 5 years (IQR: 3–7). The majority reported infertility for more than 5 years (38.2 %), followed by 3–5 years (37.2 %). The main contributing etiologic factors to infertility were primarily female factor in 568 (45.7 %) of couples, followed by unexplained factor in 292 (23.5%). Male factor was the primary cause in 310 (25.0 %), and combined factors were responsible in 72 (5.8 %) of cases according to the evaluating clinicians initial working diagnosis.

Most women had regular menstrual cycles (83.7%, n=1,040), while 202 (16.3 %) reported irregular cycles. A history of pelvic surgery was reported in one-fifth of the women (20.3 %, n=252).

The most frequent female infertility diagnoses were unexplained infertility (46.8%, n=581) and tubal factor (25.0%, n=311). These two conditions together accounted for nearly three-quarters of all diagnoses. The next most common diagnoses were Polycystic Ovary Syndrome (PCOS) (11.0%, n=137), Diminished Ovarian Reserve (DOR) (8.7%, n=108), and Premature Ovarian Failure (POF) (6.6%, n=82). Other diagnoses were rare, including uterine factor (0.5 %, n=6) and endometriosis (0.1%, n=1).

Ovarian reserve markers were documented for a subset of women. The median Anti-Mullerian Hormone (AMH) level was 0.6 ng/mL (IQR: 0.26–2.50, n=211). The median Follicle-Stimulating Hormone (FSH) was 6.8 IU/L (IQR: 5.0–9.95, n=949), and the median Antral Follicle Count (AFC) was 3 (IQR: 2–6, n=1,199).

Regarding endometrial characteristics, the majority of women (81.2 %, n=1,009) had a regular trilaminar pattern. The remaining 18.8 % (n=233) included other patterns such as trilaminar (general), shedding, and echogenic. Endometrial thickness (n=180) had a median of 6.0 mm (IQR: 5.0–7.48). Finally, assessment of tubal patency showed that three-quarters of the women (74.4 %, n=924) had bilateral patent tubes. Bilateral block was observed in 12.6 % (n=157) and unilateral block in 13.0 % (n=161). **(Table 2)**

Table 2: Reproductive history among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025(n = 1242)

Variable	Category / Value	Frequency	Percent
Type of Infertility	Primary	796	64.1
	Secondary	446	35.9
Duration of Infertility	<3 years	306	24.6
	3-5 years	462	37.2
	>5 years	474	38.2
Menstrual Cycle	Regular	1040	83.7
	Irregular	202	16.3
Pelvic Surgery	No	990	79.7
	Yes	252	20.3
Infertility Diagnosis	Tubal factor	311	25.0
	Polycystic Ovary Syndrome	137	11.0
	Diminished Ovarian Reserve	108	8.7
	Unexplained infertility	581	46.8
	Primary ovarian insufficiency	82	6.6
	Others	23	1.9
Endometrial Characteristic	Regular trilaminar	1,009	81.2
	Other patterns	233	18.8
Tubal Patency (HSG/SIS)	Bilateral Patent	924	74.4
	Bilateral Block	157	12.6
	Unilateral Block	161	13.0

5.3 . Semen Analysis Findings Semen Parameters of male partners in the study participants

5.3.1 Prevalence of Abnormal Semen Parameters

All 1,242 male partners of the studied couples underwent semen analysis. All semen analysis were classified in accordance with WHO 2021 6th edition manual semen reference standards. Among the male participants, 691 (55.6%, 95% CI= 52.9 – 58.4%) men`s semen analysis report exhibited at least one semen abnormality outside the WHO 2021 5th percentile reference range, while 551 (44.4%, 95% CI= 41.6 – 47.1%) men semen analysis had semen parameters within WHO 2021 normal ranges

5.3.2 Pattern of Semen Abnormalities

Among abnormal cases, the most common defects were: Asthenozoospermia (reduced motility): 32.5%, Oligozoospermia (low sperm concentration): 27.9%, Teratozoospermia (abnormal morphology): 17.8%. Azoospermia (no sperm): 1.0% and Akinetic sperm with no motility (0 % motility): 1.5%, also present but less frequent.

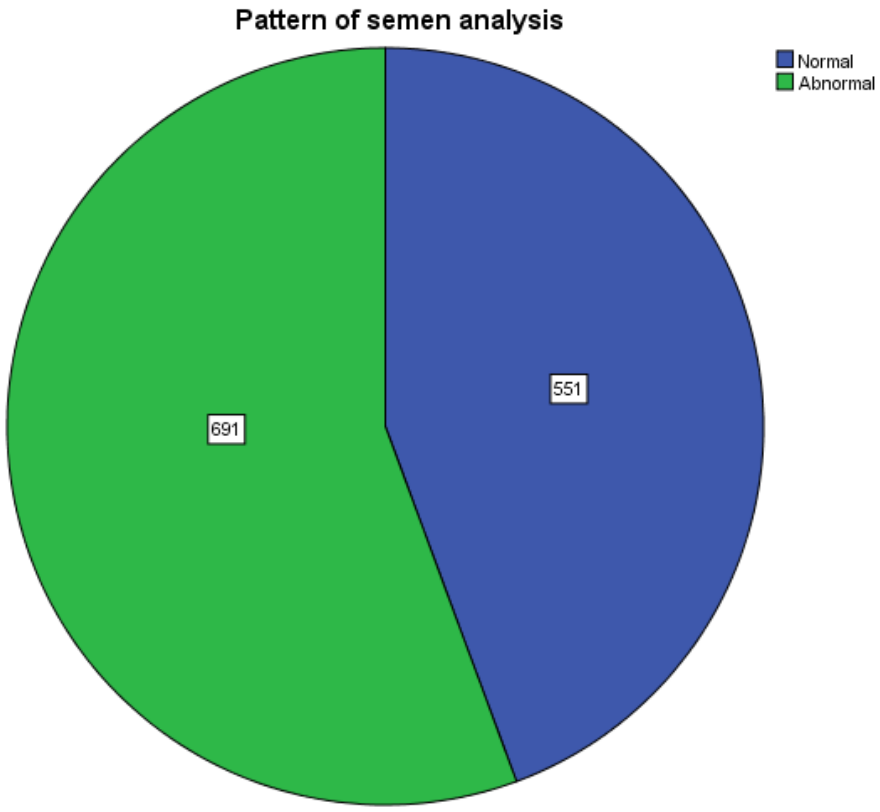
A small proportion presented with complex abnormalities such as oligoasthenoteratozoospermia (OAT).

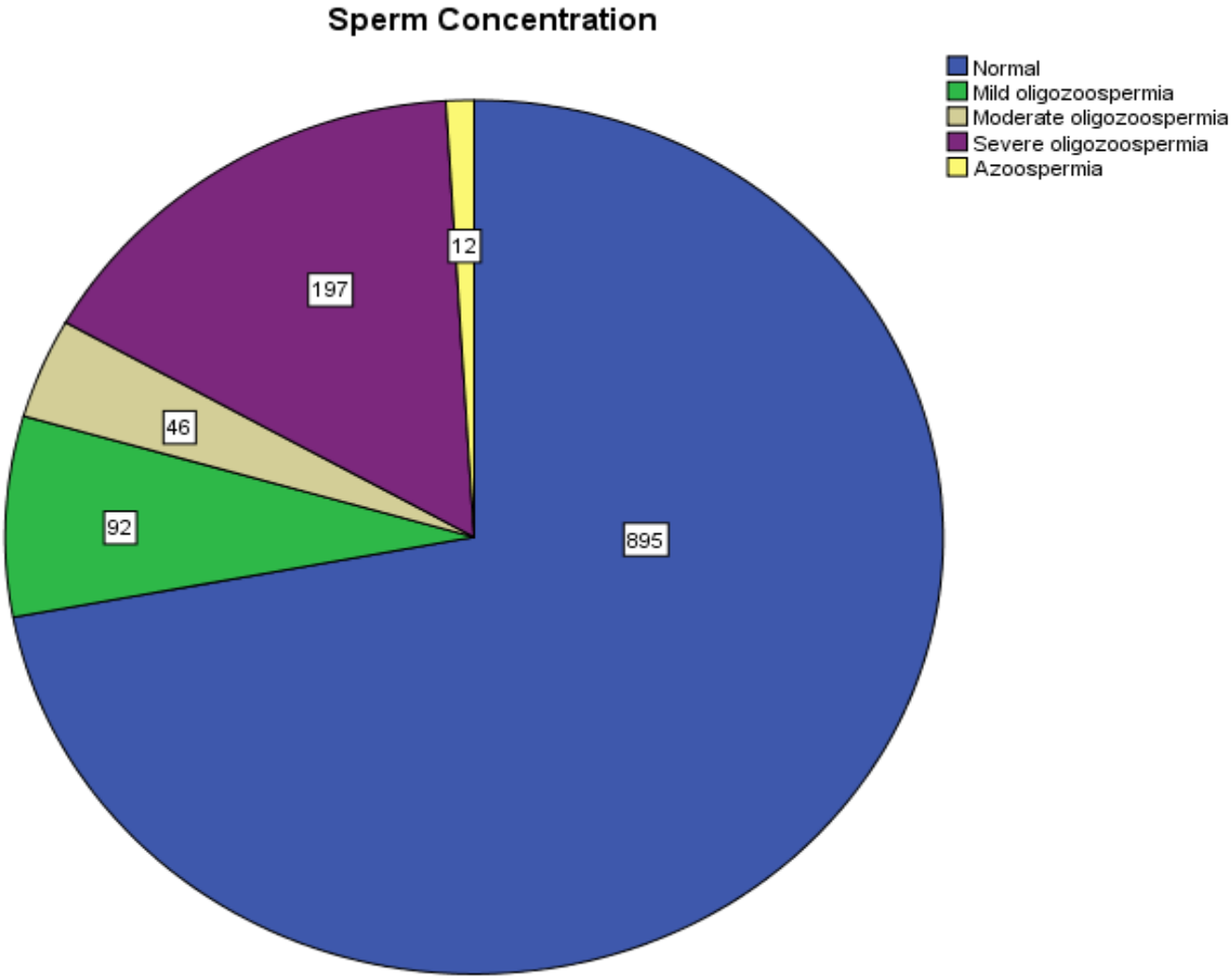
A majority of men, 895 (72.1%), had normal sperm counts (≥16 million/mL). Conversely, 347(27.9%) of men presented with some degree of oligozoospermia or azoospermia. When analyzing the distribution of low counts, severe oligozoospermia (<5.0 million/mL) was the most frequent category of abnormality, affecting 197 (15.9%) men. This was followed by mild oligozoospermia (10.0–15.9 million/mL) in 92 (7.4%) men, moderate oligozoospermia (5.0–9.9 million/mL) in 46 (3.7%) men, and azoospermia (0 sperm/mL) in 12 (1.0 %) men.

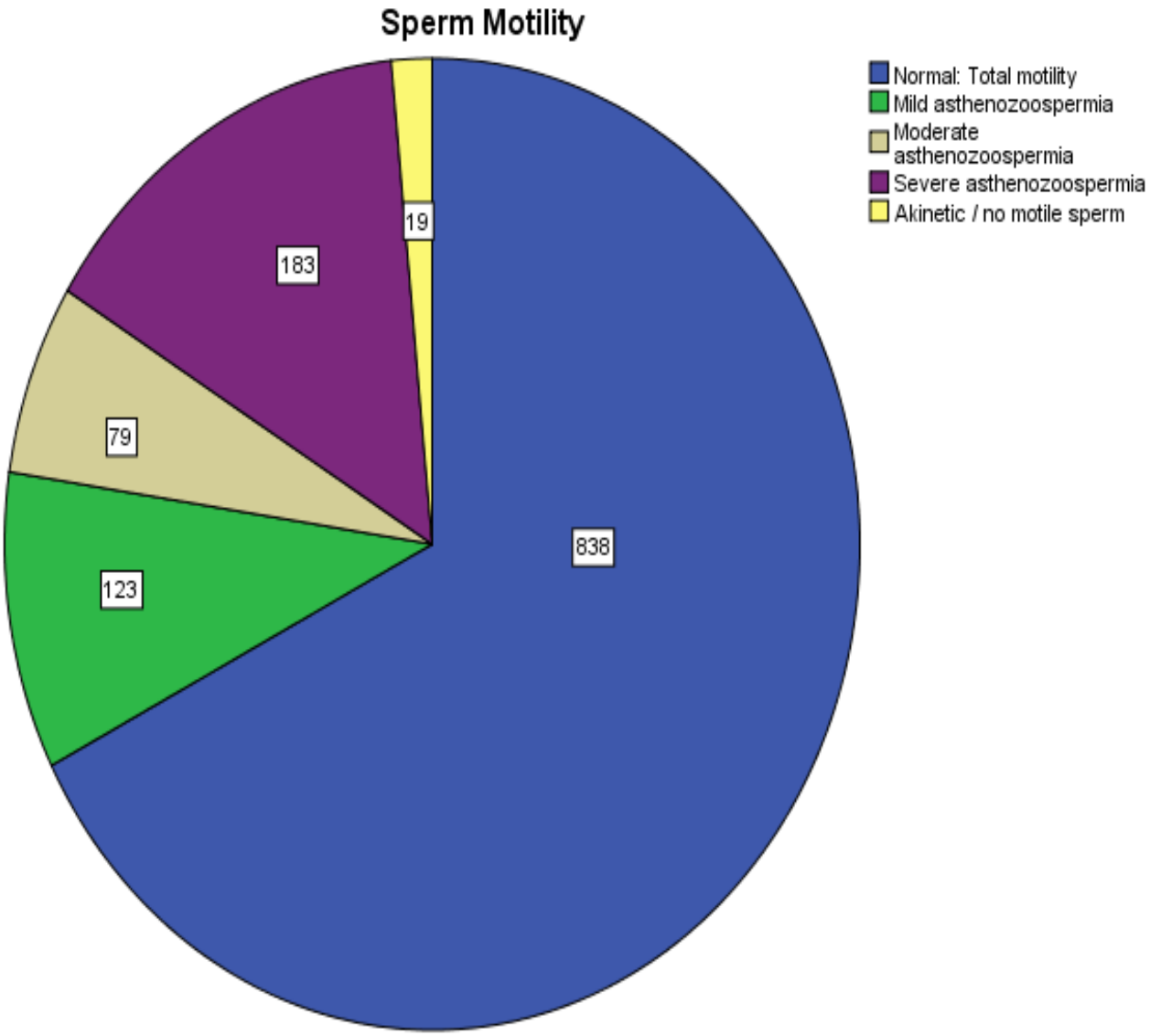
Normal total motility (≥ 42%) and progressive motility (≥ 30 %) were found in 838 (67.5%) men. Among the men with reduced motility 404(32.5%), the most prevalent finding was severe asthenozoospermia (PR <10 % or total motility <20 %), observed in 183 (14.7%) men. Mild asthenozoospermia (PR 20–29 % or total motility 32–41%) was present in 123 (9.9 %) men, moderate asthenozoospermia (PR 10–19\% or total motility 20–31 %) in 79 (6.4 %) men, and 19 (1.5%) men had no motile sperm (0 % motility).

The vast majority of men, 1,021 (82.2%), had normal sperm forms (≥ 4 %). Among those with teratozoospermia 221(17.8%), moderate teratozoospermia (1–1.9%) was the most common category, affecting 142 (11.4%) men. This was followed by mild teratozoospermia (2–3.9%) in 64 (5.2%) men, and severe teratozoospermia (<1%) in 15 (1.2%) men.

The median total motile sperm count post-wash (n=685) was 35.0 million (IQR: 14.0–60.0). Based on categorical distribution, the majority of samples (564; 82.5%) had a post-wash TMSC ≥10 million. Smaller proportions fell within lower TMSC categories, with 68 samples (9.9%) between 5–9.9 million, 44 samples (6.4%) between 1–4.9 million, and only 9 samples (1.2%) with <1 million. **(Figures 3)**




Sperm Concentration
Normal
Mild oligozoospermia
Moderate oligozoospermia
Severe oligozoospermia
Azoospermia
12
197
46
92
895


Sperm Motility
Normal: Total motility
Mild asthenozoospermia
Moderate asthenozoospermia
Severe asthenozoospermia
Akinetic / no motile sperm
838
123
79
183
19

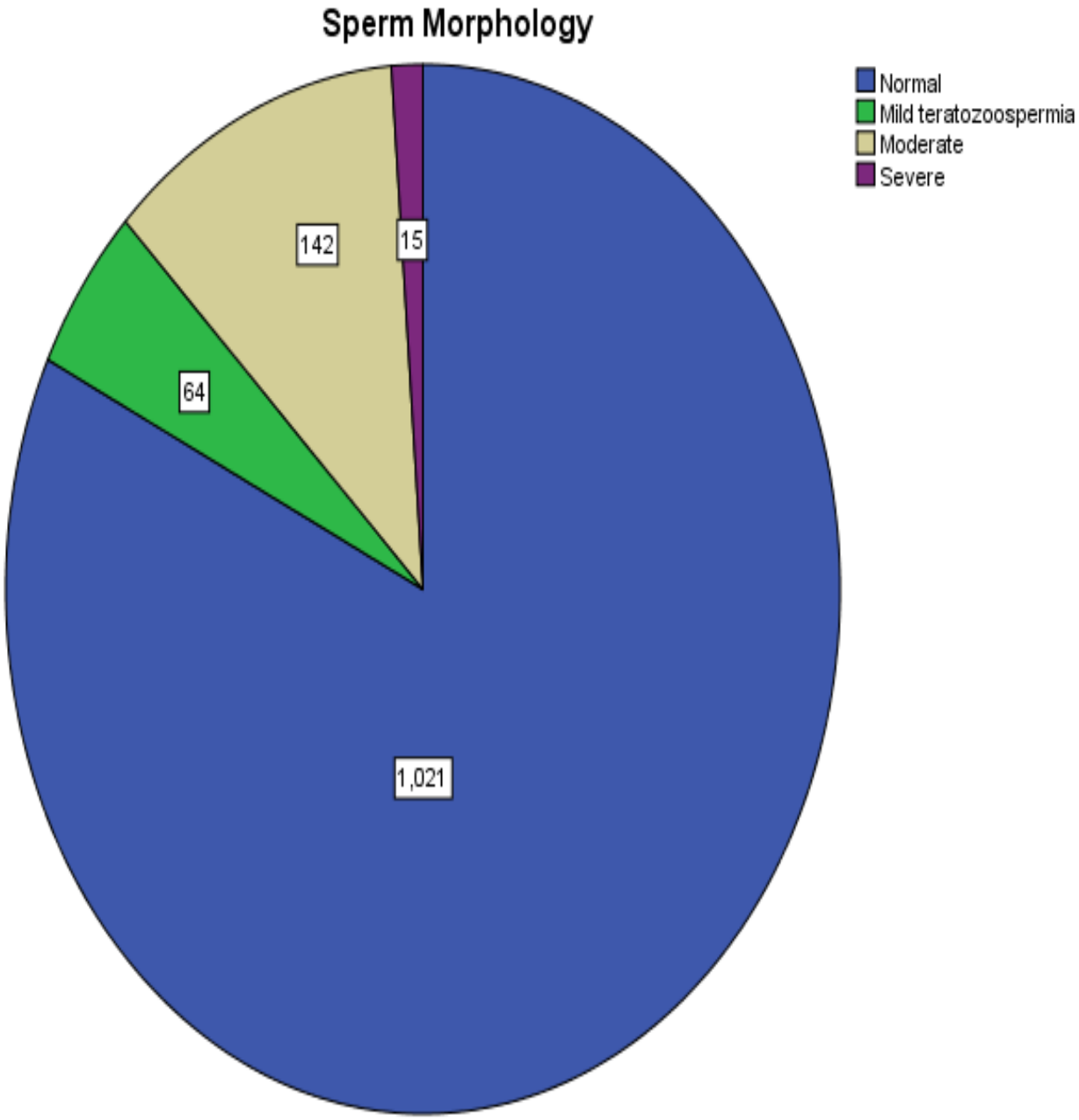


Figure 3: Prevalence of abnormal semen pattern, sperm concentration, sperm motility, and sperm morphology using WHO 2021 classification in male partners of couples receiving infertility treatment in Ethiopia between July 2021 and June 2025(n = 1242)

5.5. Comparison of Semen Abnormality patterns across different age groups and treatment year.

The distribution of specific semen parameters by both male age and year of treatment revealed clear patterns of declining semen quality with advancing age, as well as some variability across the years of treatment.

Low semen volume (<1.4 ml) increased with age, from 15.1% among men <35 years to 39.8% in men ≥45 years. Normal semen volume (≥1.4 ml) was most frequent in men aged 35–39 years (30.0%) and lowest in the oldest group (21.7%). Across treatment years, low semen volume appeared highest in 2021 (31.9%), decreased in 2024 (18.4%), and fluctuated in the intermediate years, suggesting some variability over time.

A low total sperm count (<39 million/ejaculate) was more common in older men, rising from 24.2% in men <35 years to 30.9% in those ≥45 years. Over the years of treatment, the highest proportion of low sperm count was observed in 2021 (30.2%), with some fluctuations thereafter, indicating both age- and time-related trends.

Normal sperm concentration (≥16 million/mL) decreased slightly with age, while severe oligozoospermia (<5 million/mL) increased sharply in older men (19.8% in <35 years vs. 38.1% in ≥45 years). Mild and moderate oligozoospermia showed variable distributions across age and treatment years, with notable peaks in 2023 for mild oligozoospermia (41.3%) and moderate oligozoospermia (52.2%), reflecting year-specific fluctuations in these subgroups.

Although relatively rare, azoospermia (0 sperm/mL) appeared more frequently in men ≥45 years (33.3%) and in 2024 (33.3%), indicating a concentration of this severe abnormality in older men and in later treatment years.

Normal sperm motility (total motility ≥42% and progressive motility ≥30%) was highest among younger men (<35 years: 26.4%) and declined with age (≥45 years: 22.3%). Mild, moderate, and severe asthenozoospermia all showed increasing prevalence with age, with severe asthenozoospermia reaching 38.8% in men ≥45 years. Across the treatment years, severe asthenozoospermia was most common in 2021 (36.1%) and decreased gradually to 16.4% in

2024. Akinetic sperm remained rare but was distributed across age groups and years without a clear trend.

Normal morphology (≥4% normal forms) was highest among men aged 35–39 years (28.6%) and relatively stable across years, though slightly lower in 2022 (20.7%). Moderate and severe teratozoospermia increased with age, particularly in men ≥45 years (moderate: 40.1%).

Yearly fluctuations were also evident, with the highest proportion of moderate teratozoospermia in 2021 (38.0%) and mild teratozoospermia peaking in 2021 (42.2%). Severe teratozoospermia remained uncommon across all age groups and years. **(Table 3)**

Table 3: Comparison between specific semen abnormality patterns across age and year of treatment among male partners of couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025(n = 1242)

Variable	**Male Age (years)**				**Year of treatment**			
	<35	**35-39**	**40-44**	**≥ 45**	**2021-**	**2022**	**2023**	**2024**
Semen volume								
≥ 1.4 ml	250 (26.7)	281 (30.0)	203 (21.6)	204 (21.7)	296 (31.6)	183 (19.5)	261 (27.8)	198 (21.1)
< 1.4 ml	46 (15.1)	64 (21.1)	73 (24.0)	121 (39.8)	97 (31.9)	81 (26.6)	70 (23.0)	56 (18.4)
Total sperm count								
≥ 39 * 10^6/ejaculate	184 (23.6)	228 (29.3)	185 (23.7)	182 (23.4)	253 (32.5)	174 (22.3)	203 (26.1)	149 (19.1)
< 39 * 10^6/ejaculate	112 (24.2)	117 (25.3)	91 (19.7)	143 (30.9)	140 (30.2)	90 (19.4)	128 (27.6)	105 (22.7)
Sperm concentration								

Normal: ≥ 16 million/mL	208 (23.2)	263 (29.4)	213 (23.8)	211 (23.6)	290 (32.4)	199	232	174
Mild oligozoospermia: 10.0 – 15.9 million/mL	31 (33.7)	20 (21.7)	16 (17.4)	25 (27.2)	16 (17.4)	9 (9.8)	38 (41.3)	29 (31.5)
Moderate oligozoospermia: 5.0 – 9.9 million/mL	16 (34.8)	11 (23.9)	9 (19.6)	10 (21.7)	8 (17.4)	4 (8.7)	24 (52.2)	10 (21.7)
Severe oligozoospermia: < 5.0 million/mL	39 (19.8)	47 (23.9)	36 (18.3)	75 (38.1)	76 (38.6)	49 (24.9)	35 (17.8)	37 (18.8)
Azoospermia: 0 sperm/mL	2 (16.7)	4 (33.3)	2 (16.7)	4 (33.3)	3 (25.0)	3 (25.0)	2 (16.7)	4 (33.3)
Sperm motility								
Normal: Total motility ≥ 42% AND Progressive motility (PR) ≥ 30%	221 (26.4)	242 (28.9)	188 (22.4)	187 (22.3)	250 (29.8)	166 (19.8)	241 (28.8)	181 (21.6)
Mild asthenozoospermia: PR 20–29% (or total motility 32–41%)	25 (20.3)	29 (23.6)	30 (24.4)	39 (31.7)	43 (35.0)	25 (20.3)	31 (25.2)	24 (19.5)
Moderate asthenozoospermia: PR 10–19% (or total	11 (13.9)	27 (34.2)	17 (21.5)	24 (30.4)	28 (35.4)	15 (19.0)	21 (26.6)	15 (19.0)

motility 20–31%)								
Severe asthenozoospermia: PR < 10% (or total motility <20%)	35 (19.1)	40 (21.9)	37 (20.2)	71 (38.8)	66 (36.1)	53 (29.0)	34 (18.6)	30 (16.4)
Akinetic / no motile sperm: 0% motility	4 (21.1)	7 (36.8)	4 (21.2)	4 (21.1)	6 (31.6)	5 (26.3)	4 (21.1)	4 (21.1)
Sperm morphology								
Normal: ≥ 4% normal forms	251 (24.6)	292 (28.6)	233 (22.8)	245 (24.0)	308 (30.2)	211 (20.7)	285 (27.9)	217 (21.3)
Mild teratozoospermia: 2–3.9%	16 (25.0)	17 (26.6)	11 (17.2)	20 (31.3)	27 (42.2)	12 (18.8)	16 (25.0)	9 (14.1)
Moderate: 1–1.9%	25 (17.6)	30 (21.1)	30 (21.1)	57 (40.1)	54 (38.0)	36 (25.4)	27 (19.0)	25 (17.6)
Severe: < 1%	4 (26.7)	6 (40.0)	2 (13.3)	3 (20.0)	4 (26.7)	5 (33.3)	3 (20.0)	3 (20.0)

5.6. Treatment-Related Factors of the infertile couple with Treatment Distribution

Among the couples, 635 (51.1%) had previously received fertility treatment, while 607 (48.9%) had not. The types of previous treatment included intrauterine insemination (IUI) in 279/635 couples (43.9%), intracytoplasmic sperm injection (ICSI) in 164/635 (25.9%), medical treatment with ovulation induction in 264/635 (41.6%), combinations of medical treatment with IUI or ICSI in smaller numbers, and a single case of combined medical treatment with IUI and ICSI 1/635(0.1%).

During the studied period, 685 couples (55.2%) received IUI and 557 (44.8%) underwent IVF. The main indications for IUI were female ovulatory factor (201; 29.3%), unexplained infertility (224; 32.7%), male factor (109; 15.9%), female tubal factor (92; 13.4%), and combined factor (39; 5.7%). IVF indications included male factor (206; 37.0 %), female tubal factor (204; 36.6 %), unexplained infertility (72; 12.9 %), female ovulatory factor (59; 10.6 %), and combined factor (15; 2.7 %).

Cycle types for IUI were predominantly stimulated (681; 99.4 %) with only 4 cycles out of 685 cases with IUI (0.6 %) being natural. Stimulation protocols included Letrozole in 564/685 cycles (82.3%), Clomiphene in 32 /685(4.7%), Gonadotropins in 47/685 (6.9%), combined protocols in 38 (5.5%), and gonadotropins with Antagonist protocols in all ICSI cycles 557(100.0%).

The mean number of dominant follicles for IUI group at the time of trigger was 1.56 ± 0.73 and that of the mean endometrial thickness at trigger was 8.4 mm. Insemination was performed 36 hours post-HCG in 684 cycles (99.9%) out of 685 first cycle IUIs. **(Table 4)**

Table 4: Treatment related factors among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025(n = 1242)

Variable	**Category / Value**	**Frequency**	**Percent**
Previous Fertility Treatment	No	607	48.9
	Yes	635	51.1
Current Fertility Treatment	IUI	685	55.2
	IVF-ICSI	557	44.8
First cycle IUI Treatment Indications (n=685)	Combined factor	39	5.7
	Female factor (ovulatory)	201	29.3
	Female factor (tubal)	92	13.4
	Male factor	109	15.9
	Unexplained	224	32.7

	Not documented	20	2.9
First cycle IVF-ICSI Treatment Indications (n=557)	Combined factor	15	2.7
	Female factor (ovulatory)	59	10.6
	Female factor (tubal)	204	36.6
	Male factor	206	37.0
	Unexplained	72	12.9
	Not documented	1	0.2
Stimulation Protocol for IVF-ICSI	Antagonist	557	100
Cycle Type for IUI (n=685)	Natural	4	0.6
	Stimulated	681	99.4
Stimulation Protocol for IUI (n= 685)	Clomiphene	32	4.7
	Letrozole	564	82.3
	Gonadotropins	47	6.9
	Combined	38	5.5
	Natural	4	0.6
No. of Dominant Follicles (Mean ± SD)		1.56	0.73
Insemination Timing Post-HCG	36 hours	684	99.9

5.7. Fertility Treatment Outcomes of infertile couple after first cycle IUI or ICSI

5.7.1 IUI Clinical Pregnancy Rate

Among the 685 couples who underwent first cycle IUI, 63 (9.2%) achieved pregnancy, while 595 (86.9%) did not. Biochemical pregnancy was confirmed in 63 couples (9.2%), and clinical pregnancy by transvaginal ultrasound was documented in 53 couples (7.7%) at first cycle, while 595 (86.9%) did not and the rest 27(3.9%) their outcomes were not documented on their medical chart.

Excluding the 27 couples with undocumented pregnancy outcome the proportion of biochemical pregnancy and clinically recognized pregnancies rose to 9.6% and 8.1% respectively out of 658 couples with documented pregnancy outcomes. Most pregnancies were singleton (50; 94.3%) with twin pregnancies 3 (5.7%).

The final pregnancy outcomes at discharge from clinical care or follow up was 37 ongoing viable pregnancy beyond 12 weeks of GA out of clinically recognized 53 pregnancies (69.9%), 2 ectopic pregnancies ,12 miscarriage before 12 weeks and another 2 miscarriage after 12 weeks making the ongoing clinical pregnancy rate for the IUI group 37/685 (5.4%).

Subsequent management after failed IUI included a second IUI cycle in 76 couples/595 (12.8 %), another 75 couples /595 (12.6%) attempted ICSI, and 444 couples/595 (74.6 %) were lost to follow-up. **(Table 5)**

Table 5: Fertility treatment outcomes among couples who underwent First cycle IUI treatment in Ethiopia between July 2021 and June 2025 (n = 685)

Variable	**Category / Value**	**Frequency**	**Percent**
First cycle IUI Outcome (n=685 couples)			
Tubal Patency (HSG/laparoscopy)	Bilaterally patent	579	84.5
	Unilaterally blocked	102	14.9

	Bilaterally blocked	4	0.6
TMSC (total motile sperm count)	≥10 million	564	82.5
	5–9.9 million,	68	9.9
	1–4.9 million	44	6.4
	<1 million	9	1.2
Cycle Type for IUI GROUP	Natural	4	0.6
	Stimulated	681	99.4
Pregnancy confirmed(n=685)	No	595	86.9
	Undocumented outcomes	27	3.9
	Yes, Biochemical Pregnancy	63	9.2
	Yes, Clinical Pregnancy	**53**	**7.7**
Type of clinical Pregnancy (n=53)	**Singleton**	**50**	**94.3**
	Twin	**3**	**5.7**
Final Pregnancy Outcome at discharge from clinical care and follow up (n=63/685)	**Ongoing >12 week**	**37**	**5.4**
	Biochemical loss	10	1.5
	Miscarriage <12 weeks	12	1.8
	Miscarriage >12 weeks	2	0.3
	ectopic	2	0.3
Subsequent Management After Failed IUI(n=595/685)	2nd cycle IUI	76	12.8
	ICSI	75	**12.6**
	Lost to follow up	**444**	**74.6**

5.7.2 IVF/ICSI Clinical Pregnancy Rate

Among the 557 couples undergoing first cycle ICSI, sperm was sourced from ejaculate via masturbation in 444 cases (79.7%), from testicular sperm extraction (TESE) in 112 cases (20.1%), and in 1 case (0.2%) sperm source was unknown. The GnRH antagonist stimulation protocol was used in 557 cycles (100%). The median fertilization rate was 75% (range, 50–100%).

Embryo transfer was performed in 459 cycles (82.4%), while 37 cycles (6.6%) were cancelled due to no oocytes retrieved, 3 cycles (0.5%) were cancelled due to no response, 40 cycles (7.2%) failed fertilization, and 18 cycles (3.2%) did not have an embryo to transfer. Embryo transfer stages included Fresh Day 3 in 324 cycles (70.7%), Fresh Blastocyst Day 5 in 65 cycles (14.2%), and Frozen Day 5 in 69 cycles (15.1%). The number of embryos transferred included one embryo in 90 cycles (19.7%), two embryos in 232 cycles (50.7%), and three embryos in 136 cycles (29.7%). Endometrial thickness at transfer had a mean of 9.91 mm (± 2.39).

Out of 557 cases with IVF/ICSI biochemical pregnancy was observed in 142 cycles (25.5%) of which clinical pregnancy on ultrasound confirmed in 106 cycles (19.0%) and 36 cycles (6.5%) ended up with biochemical loss. While 415/557(74.5%) treatment cycles ICSI with ET showed no biochemical or clinical pregnancy. Most pregnancies were singleton (89; 84.0%) with twin pregnancies 17 (16.0%).

The final pregnancy outcomes at discharge from clinical care or follow up is 97/557 (17.4%) ongoing pregnancy beyond 12 weeks of GA. Subsequent management after failed ICSI-ET 64 couples (15.4%) out of 415 treatment cycles re attempted second ICSI, while 351 (84.6 %) were lost to follow-up. **(Table 6)**

Table 6: Fertility treatment outcomes among couples who underwent First-Cycle ICSI treatment in Ethiopia between July 2021 and June 2025 (n = 557)

Variable	**Category / Value**	**Frequency**	**Percent**
First Cycle ICSI Characteristics			
Sperm Source	Ejaculate	444	79.7
	TESE	112	20.1
	Unknown	1	0.2
Fertilization Rate (Median [IQR])	-	75.0	50-100.0
ICSI Cycle Outcome	**Embryo Transferred**	**459**	**82.4**
	Cancelled / No Oocyte	37	6.6
	Failed Fertilization	40	7.2
	Cancelled/no response	3	0.5
	No embryo transfer	18	3.2
Embryo Transfer Stage (n=459)	Fresh Day 3	324	70.7
	Fresh Blastocyst Day 5	65	14.2
	Frozen Day 5	69	15.1
Embryos Transferred (n=459)	One	90	19.7
	Two	232	50.7
	Three	136	29.7
Pregnancy confirmed (n= 557)	No	415	74.5

	Yes	142	25.5
	Biochemical	**142**	**25.5**
	Clinical	**106**	**19.0**
Type of clinical Pregnancy (n=106)	Singleton	89	84.0
	Twin	17	16.0
Final Pregnancy Outcome at discharge from clinical care and follow up (n=142/557)	**Ongoing > 12week**	**97**	**17.4**
	Biochemical loss	36	6.5
	Miscarriage < 12 week	7	1.3
	Miscarriage >12week	2	0.4
	Ectopic	2	0.4
Subsequent Management After Failed ICSI-ET (n=415)	2nd cycle ICSI	64	15.4
	Lost to follow up	351	84.6
	Total	415	**100.0**

5.8. The comparative treatment outcome of infertile couples per treatment modality options and semen analysis pattern

The analysis of the distribution of pregnancy outcomes among couples who underwent first cycle IUI and ICSI, stratified by semen quality shows the following. Among couples treated with first cycle IUI, 49.9% had normal semen and 50.1% had abnormal semen. Pregnancy occurred in 28 couples (8.2%) with normal semen and in 25 couples (7.3%) with abnormal semen. Conversely, the majority of couples in both groups did not achieve pregnancy (91.8% for normal semen and 92.7% for abnormal semen).

For couples undergoing first cycle ICSI, 37.5% had normal semen and 62.5% had abnormal semen. Pregnancy rates were higher in ICSI cycles compared to IUI, with 38 couples (18.2%) achieving pregnancy in the normal semen group and 68 couples (19.5%) in the abnormal semen group. Non-pregnancy rates were 81.8% and 80.5% for the normal and abnormal semen groups,

respectively**.** **(Figure4)**

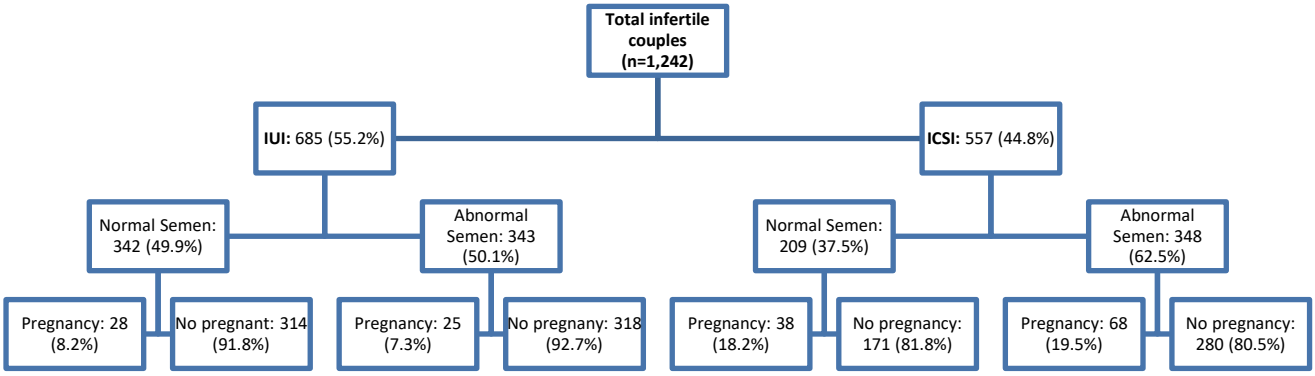


Figure 4: Fertility treatment outcomes per treatment type and semen parameter status among couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

5.9 Comparison Between Semen Abnormality and Clinical Characteristics

A comparison of baseline characteristics between men with normal and abnormal semen analysis revealed several significant differences.

The semen pattern analysis across years of treatment showed a statistically significant trend ($p = 0.046$) where the proportion of abnormal results increased progressively over time from 50.1% in 2021 to 56.1% in 2022, 58.3% in 2023, and rising to 60.2% in 2024. This pattern suggests a gradual shift toward a higher prevalence of abnormal semen profiles in more recent years. Increasing male age was associated with a higher prevalence of abnormal semen parameters. While semen abnormalities were distributed across all age categories, the proportion was greatest in men aged ≥45 years (62.2%) and lowest among those <35 years (53.0%) ($p=0.048$). **(Figure 5)**

The duration of infertility did not show a significant association with semen abnormality ($p = 0.464$), with similar distributions across categories. However, semen abnormality was significantly more common among couples with primary infertility (59.2%) compared to those with secondary infertility (49.3%) ($p = 0.001$).

Male pelvic or inguinal surgery was strongly associated with abnormal semen parameters. Among men with a history of surgery, 97.4% had abnormal semen results compared to 51.4% of those with no surgical history ($p < 0.0001$).

The type of current treatment also varied significantly by semen status. Abnormal semen analysis was more common among couples undergoing ICSI (62.5%) than those undergoing IUI (50.1%) ($p < 0.0001$).

Clinical pregnancy rates did not significantly vary by semen abnormality, both overall and when stratified by treatment type. Among IUI cycles, of the 53 cycles with a confirmed clinical pregnancy, 28 (52.8%) had normal semen and 25 (47.2%) had abnormal semen, while among the 632 cycles without clinical pregnancy, 314 (49.7%) had normal semen and 318 (50.3%) had abnormal semen. There was no statistically significant difference in clinical pregnancy by semen status among IUI cycles ($p = 0.660$).

For ICSI cycles, of the 106 cycles with a confirmed clinical pregnancy, 38 (35.8%) had normal semen and 68 (64.2%) had abnormal semen, while among the 451 cycles without clinical pregnancy, 171 (37.9%) had normal semen and 280 (62.1%) had abnormal semen. Similar with the IUI findings, there was also no statistically significant difference in the clinical pregnancy rate based on the male partner's semen status among the ICSI cycles (p = 0.693). **(Table 7)**

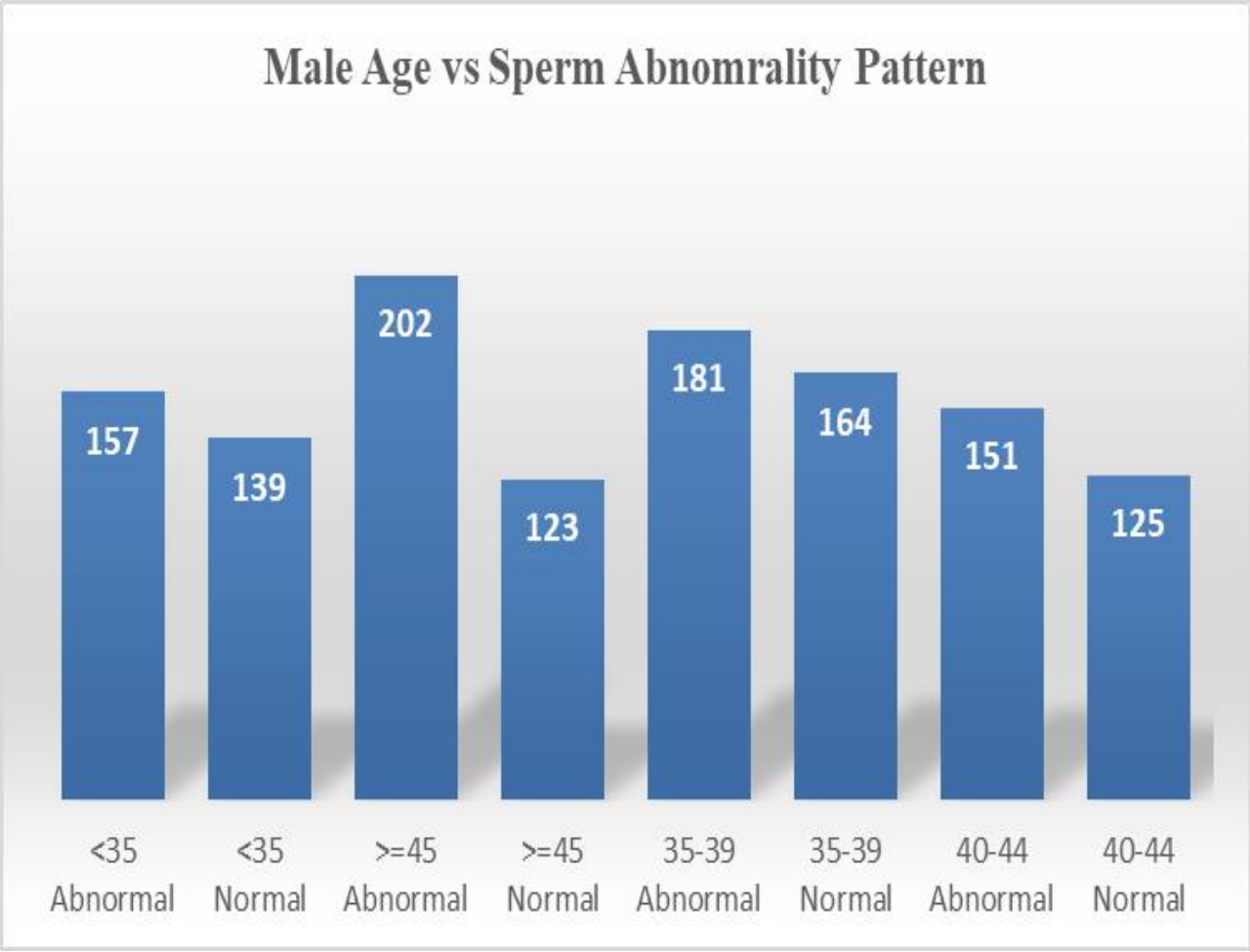


Figure 5: Semen abnormality patterns per age group in male partners of couples receiving infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Table 7: Comparison between specific semen abnormality and clinical characteristics among male partners of couples who underwent infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

Variable	Semen analysis		p-value
	Normal (%)	Abnormal (%)	
Year of treatment			
2021	196 (49.9)	197 (50.1)	**0.046***
2022	116 (43.9)	148 (56.1)	
2023	138 (41.7)	193 (58.3)	
2024	101 (39.8)	153 (60.2)	
Male Age			
<35	139 (47.0)	157 (53.0)	**0.048***
35-39	164 (47.5)	181 (52.5)	
40-44	125 (45.3)	151 (54.7)	
>=45	123 (37.8)	202 (62.2)	
Duration of infertility (in years)			
< 3	145 (47.4)	161 (52.6)	0.464
3-5	199 (43.1)	263 (56.9)	
>5	207 (43.7)	267 (56.3)	
Type of infertility for the couple			
Primary	325 (40.8)	471 (59.2)	**0.001***
Secondary	226 (50.7)	220 (49.3)	
Pelvic/inguinal surgery (male)			
No	548 (48.6)	580 (51.4)	**<0.0001***
Yes	3 (2.6)	111 (97.4)	
Current treatment modality			
IUI	342 (49.9)	343 (50.1)	**<0.0001***
ICSI	209 (37.5)	348 (62.5)	
Clinical pregnancy (Total)			
No	485 (44.8)	598 (55.2)	0.438
Yes	66 (41.5)	93 (58.5)	
Clinical pregnancy (IUI) (n=685)			
No	314 (49.7)	318 (50.3)	0.660
Yes	28 (52.8)	25 (47.2)	
Clinical pregnancy (ICSI) (n=557)			
No	171 (37.9)	280 (62.1)	0.693
Yes	38(35.8)	68(64.2)	

5.10. Comparison of pregnancy outcomes between specific Semen Abnormality patterns below the WHO 2021 reference limits and normal semen parameters

This analysis compares clinical pregnancy outcomes across various semen parameters in a cohort of 1,242 men. Notably, several semen parameters falling below the WHO 2021 reference limits were associated with proportionally higher clinical pregnancy rates (CPR) than those within the normal range.

Volume & Count: Of the 304 men (24.5%) with low semen volume (<1.4 mL), 16.4% achieved pregnancy, compared to 11.6% of men with normal volume. While 62.7% of men had a normal total sperm count (≥39 million), their CPR was 12.3%. In contrast, men with a subnormal count (<39 million) had a slightly higher CPR of 13.6%.

Morphology & Azoospermia: From a total of 1242 semen analysis reports 1021(82.2%) were having normal sperm forms. A higher CPR was found in men with abnormal sperm morphology (16.7%) versus those with normal forms (11.9%). Among 12 men with azoospermia, four (25.0%) achieved pregnancy via ICSI using sperm retrieved surgically. **(Figure 6)**

Concentration & Motility: A large proportion of men, 779(62.7%) were also found to have a normal total sperm count of greater than or equal to 39 million. A CPR of 15.0% was observed among men with low sperm concentration (<16 million/mL), versus 12.0% for those with normal concentration. Out of 1242 men ,404 men with reduced motility consisting of 32.5% the studied semen analysis reports and the rest 838(67.5%) were having normal sperm motility with in the reference range as per 2021WHO recommendation. Similarly, for motility, men with suboptimal motility (<42%) had a CPR of 15.8%, compared to 11.3% for men with normal motility (≥42%). This includes five pregnancies from 19 men with completely no motile sperm). **(Figure 7)**

In this study population, suboptimal semen parameters were consistently linked with proportionally higher clinical pregnancy rates than parameters within the standard WHO reference ranges.

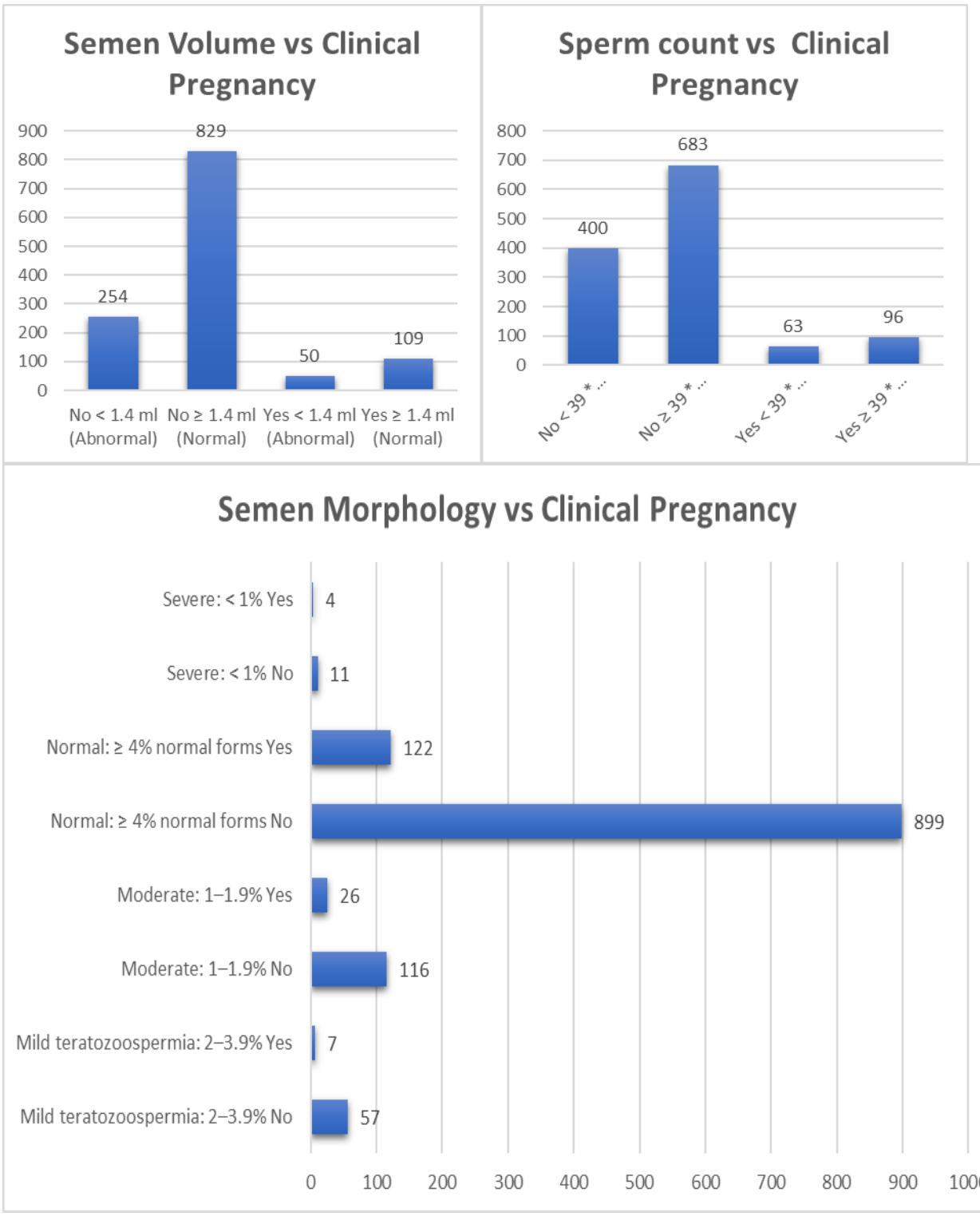


Figure 6: CPR-among couples receiving fertility treatment per semen volume,count and morphology status in Ethiopia between July 2021 and June 2025 (n = 1242)

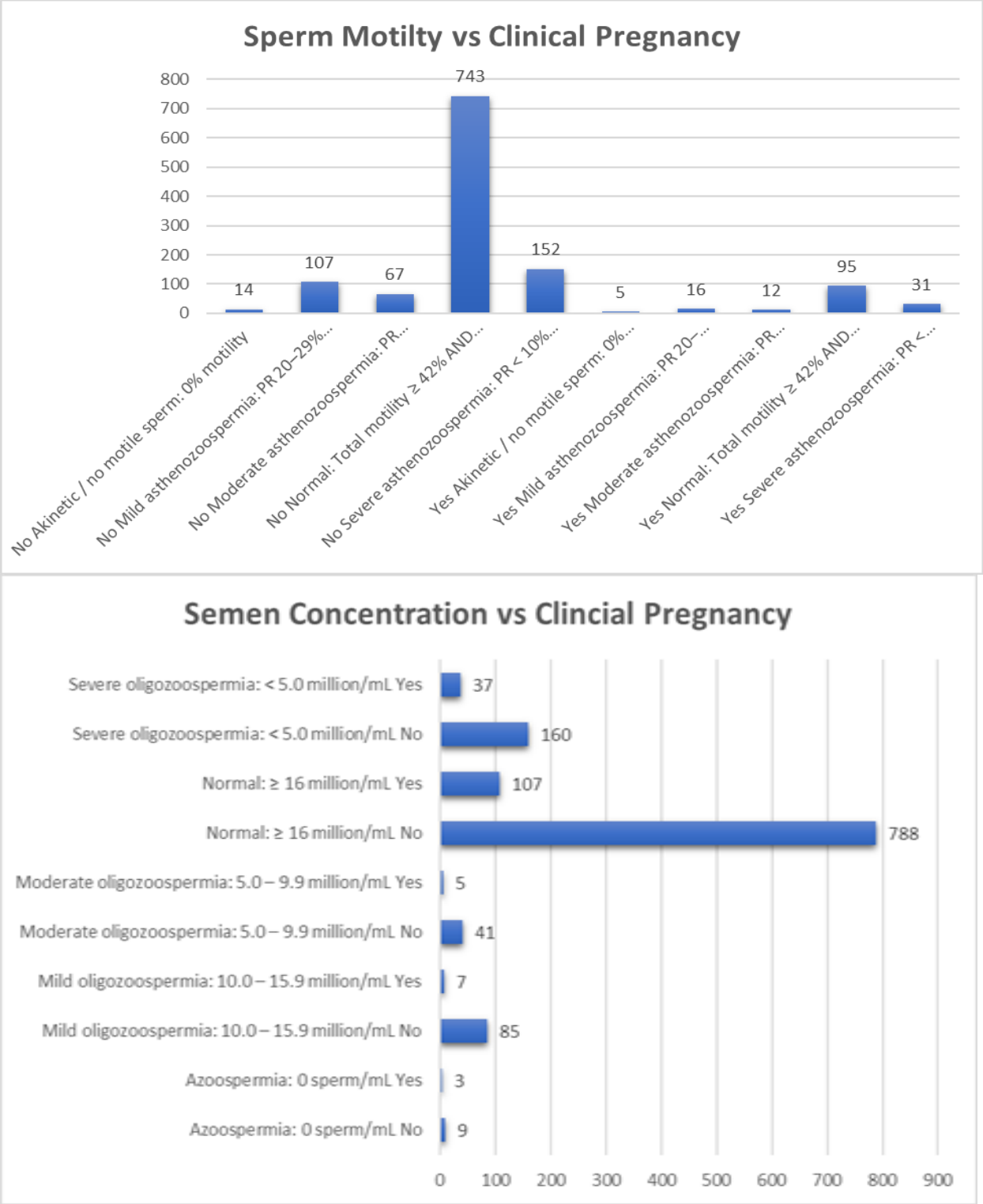


Figure 7: CPR-among couples receiving fertility treatment per semen concentration and sperm motility status in Ethiopia between July 2021 and June 2025 (n = 1242)

5.11 Clinical pregnancy rate

Among all treatment cycles, 159 cases (12.8%, 95% CI= 11.0 – 14.7%) had a confirmed clinical pregnancy by TVS, while 1,083 cases (87.2%, 95% CI= 85.3 – 89.0%) did not. When examined by treatment modality, clinical pregnancy was more frequently achieved in ICSI cycles than in IUI cycles. Among the 685 IUI cycles, only 53 (7.7%) resulted in a clinical pregnancy, whereas 632 (92.3%) did not. In contrast, among the 557 ICSI cycles, 106 (19.0%) achieved clinical pregnancy, with the remaining 451 (81.0%) showing no clinical pregnancy.

Clinical pregnancy rates were also examined in relation to semen quality A similar pattern was observed when semen quality was categorized using WHO 2021 reference criteria. Of the cycles without clinical pregnancy, 598 had abnormal semen and 485 had normal semen. Among cycles with confirmed clinical pregnancy, 93 occurred in the abnormal semen group and 66 in the normal group. Although abnormal semen parameters were more common overall, proportionally higher pregnancy rates (13.5% vs 12.0%) were again seen among men with abnormal semen. **(Figure 8)**

Overall documented clinical pregnancy outcomes were available for 1,215 including 98 IVF/ICSI cycles that did not proceed to embryo transfer which were by definition non-pregnant, accounting to 97.8% of the 1,242 initiated cycles. The clinical pregnancy rate within this cohort of documented outcomes is 13.1% (159/1,215). Among documented cycles, complete-case analysis, the clinical pregnancy rate was 8.1% (53/658) for IUI and 19.0% (106/557) for IVF/ICSI cycles.

To assess the robustness of the IUI outcome, a sensitivity analysis was performed on the 27 IUI cycles with undocumented results. Assuming all undocumented cases were failures, the IUI pregnancy rate would be 7.7% (53/685). Assuming all were successes, the rate would be 11.7% (80/685). Our primary analysis result of 8.1% falls within this range.

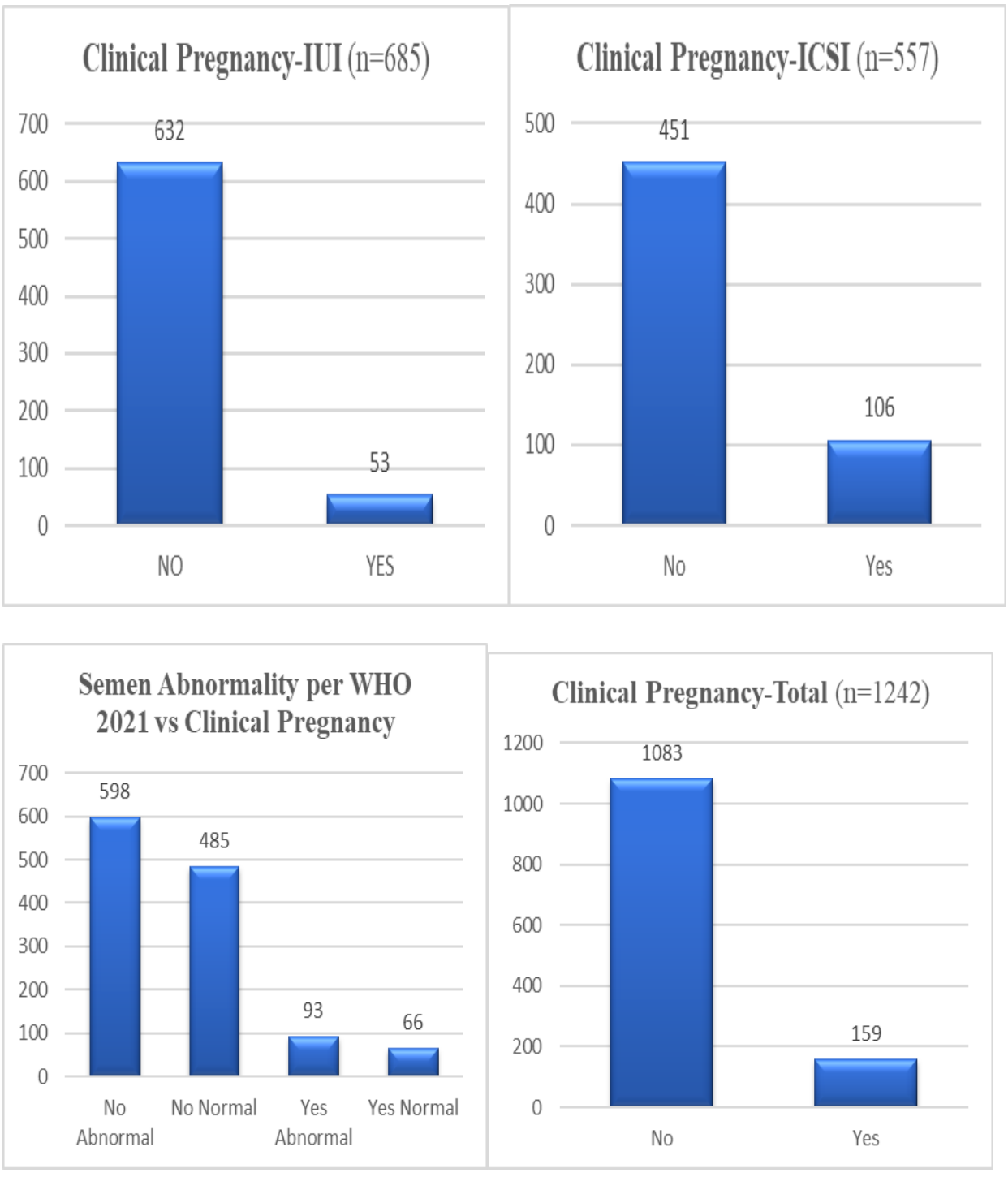


Figure 8: Clinical pregnancy rate among couples receiving infertility treatment in Ethiopia between July 2021 and June 2025 (n = 1242)

5.12 Determinants of clinical pregnancy

From the univariate analysis, female factors, male age, male chronic illness, male pelvic/inguinal surgery, sperm parameters, duration of infertility, previous fertility treatment, and current fertility treatment types were found to be significant and were fitted into the final regression model, the multivariable binary logistic regression model. The goodness-of-fit of the final logistic regression model was assessed using the Hosmer–Lemeshow test. The result was non-significant ($\chi^2 = 4.266$, df = 8, p = 0.832), indicating that the model fitted the data adequately.

In the multivariable binary logistic regression analysis, after adjusting for other confounding factors, female age and current fertility treatment type were identified to be the only significant determinants of the occurrence of clinical pregnancy.

Women aged 35 years and older had 56% lower odds of achieving clinical pregnancy compared to women younger than 30 years (AOR = 0.44, 95% CI= 0.27–0.74, p-value = 0.002). In contrast, women aged 30–34 years did not differ significantly from those under 30 years. In addition, couples who underwent IVF-ICSI had 3.65 times higher odds of clinical pregnancy compared to those receiving IUI (AOR = 3.65, 95% CI= 2.31–5.78, p-value= < 0.0001).

On the other hand, semen parameter abnormality did not show any significant relationship with the clinical pregnancy rate after controlling for other confounders in this cohort. **(Table 8)**

Table 8: Determinants of clinical pregnancy among couples who underwent infertility treatment in Ethiopia between 1 January 2021 and 31 December 2024 (n = 1242)

Variable	**Category**	**Clinical Pregnancy**		**COR (95% CI)**	**AOR (95% CI)**	**p-value**
		No	**Yes**			
Female Factors						
Age (years)	<30	232	49	1	1	
	30–34	288	53	0.87 (0.57, 1.33)	0.78 (0.49, 1.26)	0.312
	≥35	563	57	0.48 (0.32,	**0.44 (0.27,**	**0.002**

				0.72)	**0.74)**	*
Chronic Medical Illness	No	1027	154	1	1	
	Yes	56	5	0.59 (0.24, 1.51)	0.67 (0.25, 1.81)	0.431
Menstrual Cycle	Regular	910	130	1	1	
	Irregular	173	29	1.17 (0.76, 1.81)	1.51 (0.95, 2.39)	0.085
Pelvic Surgery	No	863	127	1	1	
	Yes	220	32	0.99 (0.65, 1.49)	1.03 (0.66, 1.63)	0.886
Tubal Patency (HSG/Laparascopy)	Bilateral Patent	811	113	1	1	
	Unilateral Block	143	18	0.90 (0.53, 1.53)	0.97 (0.56, 1.69)	0.918
	Bilateral Block	129	28	1.56 (0.99, 2.45)	0.91 (0.53, 1.57)	0.743
Male Factors						
Age (years)	<35	251	45	1	1	0.616
	35–39	295	50	0.95 (0.61, 1.46)	1.18 (0.73, 1.92)	0.494
	40–44	243	33	0.76 (0.47, 1.23)	1.06 (0.61, 1.85)	0.832
	≥45	294	31	0.59 (0.36, 0.96)	0.83 (0.46, 1.51)	0.546
Chronic Medical Illness	No	990	123	1	1	
	Yes	93	36	0.89 (0.50, 1.56)	1.22 (0.65, 2.28)	0.539
Pelvic/Inguinal	No	990	138	1	1	

Surgery	Yes	93	21	1.62 (0.98, 2.69)	0.93 (0.42, 2.03)	0.848
Sperm Concentration (presence of oligozoospermia)	Normal	788	107	1	1	
	Mild	85	7	0.61 (0.27, 1.35)	0.69 (0.30, 1.61)	0.394
	Moderate	41	5	0.89 (0.35, 2.32)	0.87 (0.31, 2.44)	0.788
	Severe	169	40	1.74 (1.17, 2.59)	1.41 (0.58, 3.44)	0.446
Sperm Motility (presence of asthenozoospermia)	Normal	743	95	1	1	
	Mild	107	16	1.17 (0.66, 2.06)	1.19 (0.65, 2.18)	0.582
	Moderate	67	12	1.40 (0.73, 2.68)	1.42 (0.68, 2.94)	0.349
	Severe	166	36	1.69 (1.12, 2.58)	1.29 (0.53, 3.18)	0.570
Sperm Morphology (presence of teratozoospermia)	Normal	899	122	1	1	
	Mild	57	7	0.91 (0.40, 2.03)	0.43 (0.15, 1.25)	0.122
	Moderate – Severe	127	30	1.74 (1.12, 2.7)	0.54 (0.16, 1.84)	0.326
Couple-Level Factors						
Duration of Infertility (years)	<3	264	42	1	1	
	3–5	395	67	1.07 (0.70, 1.62)	1.03 (0.67, 1.58)	0.910
	>5	424	50	0.74 (0.48, 1.15)	0.66 (0.41, 1.05)	0.080
Previous Fertility Treatment	No	533	74	1	1	
	Yes	550	85	1.11 (0.79,	1.04 (0.72,	0.839

				1.55)	1.49)	
Current Treatment Type	IUI	632	53	1	1	
	IVF-ICSI	451	106	2.80 (1.97, 3.98)	**3.65 (2.31, 5.78)**	**<0.001***

Note: COR, Crude odds ratio; AOR, Adjusted odds ratio; CI, Confidence interval; *****statistically significant

6. DISCUSSION

6.1. Overview of Main Findings

This study assessed the prevalence, patterns, and treatment outcomes of abnormal semen parameters among 1,242 infertile couples evaluated at two major fertility centers in Addis Ababa over a four-year period with first-cycle IUI and ICSI attempt. The study findings give land mark local evidence about semen abnormalities and reproductive outcomes in relation with male factor infertility in Ethiopia where literature remains limited. This chapter discusses the key findings in relation to the study objectives and compares them with existing global and regional evidence. Our findings highlight the significant burden of possible male factor infertility and provide insight into the effectiveness ART service in this setting.

This four-year retrospective study of 1,242 infertile couples represents the largest and most detailed dataset on semen parameter abnormalities and ART outcomes reported from Ethiopia to date. About half (55.6%) of male partners were found to have an abnormal semen parameter outside WHO 2021 reference range in at least one of the major sperm parameters. ICSI achieved markedly higher pregnancy rates than IUI, with biochemical pregnancy rates of 25.5% vs 9.2% and clinical pregnancy rates of 19.0% vs 7.7%, respectively. After adjusting for confounders, semen abnormalities were not independently associated with clinical pregnancy, whereas female age ≥35 years and treatment modality with ICSI were strong predictors of success. High loss to follow-up (444/595)—74.6% after failed IUI and 84.6% after failed ICSI (351/415)—highlighted significant barriers to continuity of care.

6.2. Prevalence and Patterns of Abnormal Semen Parameters

Among the 1,242 couples included, a substantial proportion of male partners exhibited abnormal semen parameters (55,6%), lower than previous Ethiopian and Middle East studies reporting male factor infertility in 64–84% of infertile couples (39,44,49), and higher than the pooled prevalence of 22.26% of male-related problems reported by Abebe et al (37). The difference in prevalence may be the larger sample size of the study participants in addition to the use of the updated WHO 2021 manual for classification which overestimates suboptimal semen parameters in our study participants.

The prevalence of abnormal semen parameters (55.6%) in this study is slightly higher than the global range of 30–50% and is in agreement with estimates attributing male factors to 20–50% of infertility cases worldwide (19). It is consistent with sub-Saharan African reports where male or combined male–female factors contribute 40–60% of infertility (37). However, our study demonstrated a notably high burden of severe sperm defects, but azoospermia accounted for 1.0% of cases — both lower than many African series (6–15%) (10,35,38,40,54) this low percentage of azoospermia in our study may be due to higher incidence of STI causing obstructive azoospermia with epididymal obstruction. STIs are more common in the low socioeconomic group of the community who are unlikely to visit the private fertility centers for financial reasons where we conducted our study.

The findings from this study can be directly compared with and contextualized by the 2021 SPHMMC unpublished study (44), which utilized the WHO 2010 criteria. While this present study, employing the updated WHO 2021 criteria, found a semen abnormality prevalence of 55.6%, the earlier SPHMMC study reported a slightly higher rate of 62.4% in a similar tertiary hospital population in Addis Ababa. This difference, though not large, could reflect natural variation between cohorts, differences in the underlying patient population, or potentially the impact of using different WHO reference editions.

Contrary to findings in SPHMMC study which found 33.9% of azoospermia and also the 24 .0% azoospermia prevalence in west Welega study, our study found only a small proportion of men 12 (1.0%) had azoospermia with no sperm in their sample (39,43). This huge discrepancy may highlight how patient selection and referral patterns to specialized public IVF center and faith-based health institute in Welega significantly shaped the observed clinical profile in male factor infertility even in same city and country respectively. Our azoospermia prevalence is also notably lower than global averages (~10%) this may be as a result of the low prevalence of varicocele (0.4%) in our study population as compared to other studies.

Severe oligozoospermia as defined by sperm count of less than 5 million per ml comprised of almost 16 % of the infertile couple which is comparable to previous Asian and African studies (39). Suboptimal motile sperms below the WHO 5^{th} percentile accounting for 32.5% and sperm count outside the WHO 5^{th} percentile comprising almost 28.0% were the most common isolated

abnormalities which is in agreement with a comparable finding from Abebe et al. (37), and similar regional analyses. A possible explanation for these larger proportions of abnormal semen parameters in male factor infertility in this study may be as a result of prolonged duration of infertility with the median duration observed from this study being 5 years. Another possible explanation might be delayed presentation to higher level specialty care and also local determinants including under recognized risk factors such as environmental/occupational heat exposures, life style factors, previous genital infections, untreated and undiagnosed varicocele (14,20,30).

In general, the prevalence observed in this study is slightly lower than some East African reports but higher than Western population-based studies, likely reflecting differences in healthcare access, late presentation, environmental exposures, and prevalence of untreated infections. The use of strict WHO 2021 semen reference values, which raised thresholds for motility and morphology, may also contribute to the relatively high abnormality rates in our study.

These findings align with global patterns, where reduced sperm concentration and motility are the leading contributors to possible male infertility. The relatively high prevalence of male factor infertility emphasizes the need for routine semen analysis in infertility workups and early identification of sub fertile men. The higher proportion of azoospermia in other studies may also reflects referral bias to specialized ART centers capable of offering TESE, which was used in 9.0% of ICSI cycles in this cohort but azoospermia was low only in (12)1.0%.

6.3. The role of semen parameters on pregnancy outcome in ART

Several semen parameters commonly associated with poor outcomes like low concentration, low motility and low morphology interestingly did not strongly predict clinical pregnancy rates in this study. This observation might reflect of the dominant role of assisted reproductive technologies (ICSI) overcoming barriers to pregnancy from severe male factor semen abnormalities. The ASRM and AUA guidelines clearly note that ICSI effectively bypasses limitations imposed by sperm count, morphology and motility which is consistently in agreement with our findings (3).

. The AUA/ASRM guidelines note that ICSI effectively bypasses limitations imposed by sperm count, motility, and morphology (3). In a similar way, our findings that semen parameters were not independent predictors of clinical pregnancy actually resonates well with the WHO 2021's key message that numerical values alone are insufficient for diagnosis or prognosis rather infertility should be seen from both partners clinical condition or perspective. (15,59)

The main findings of this cross-sectional study are in agreement with a growing body of evidence that challenges the independent prognostic power of standard semen analysis for ART success like clinical pregnancy which is a closer surrogate of live birth. Consistent with the study (51), Our analysis of 1,242 couples, consistent with the study (51) found that clinical pregnancy rates (CPR) were not consistently lower in groups with abnormal parameters; in some cases of infertile couple, proportions were comparable or even higher than in those couples with normal semen profiles according to WHO 2021 reference criteria. This strengthens the concept that while semen parameters are critical for diagnosing the need for ART and triaging what type of ART is needed, they may not be strong independent predictors of success in clinical pregnancy once fertilization is achieved, particularly with ICSI.

Findings from our study, coupled with the existing literature globally, indicate that the journey from abnormal sperm to a clinical pregnancy is governed by other clinical factors, mainly female age with good oocyte quality and favorable endometrial receptivity, which can compensate for or override paternal contributions at later stages of embryo development. Therefore, the clinical focus need shift from viewing isolated semen parameters as definitive outcome predictors to integrating them into a broader diagnostic and prognostic framework that prioritizes female factors and embryo quality for prognosticating ART success at individual level for each couple.

Other findings from a study (53) similarly offer a critical framework for interpreting the primary results and findings of the present study strongly supporting the conceptual model of embryo development. After successful fertilization through ICSI procedures, the developmental potential of the resulting embryo and its subsequent implantation into the sub endometrial space is moderated predominantly by oocyte competence and endometrial receptivity. Findings from this study agrees with the observation that variations in traditional semen characteristics may have a diminished role and influence on later-stage embryogenesis and clinical outcomes in ART.

The apparent limited predictive value of male factors such as age and semen analysis in blastocyst quality and pregnancy success in many studies including this study, therefore may be best understood not as an absence of impact, but as a demonstration of ICSI`s ability to circumvent many sperm-related barriers to fertilization. The central clinical implication is that treatment strategies should fundamentally prioritize optimizing oocyte quality and the uterine environment, as therapeutic interventions targeting standard and conventional parameters alone are unlikely to yield significant improvements in ICSI success rates once a viable sperm sample is identified and secured for IVF/ICSI

6.4. IUI Outcomes and Their Clinical Context

The clinical pregnancy rate following IUI was 7.7%, which is within the internationally expected range of 6–12% per stimulated cycle but lower than high-performing centers reporting 12–18% (3,24,49). A major contributing factor appears to be patient selection in our study population where a considerable proportion of IUI patients had unexplained infertility or potential female factor issues—groups known to have modest success with IUI.

Although the median post-wash TMSC was high (35 million), indicating adequate sperm quantity, IUI outcomes remained suboptimal in this study. This could be due to not adhering to well established international guidelines including WHO 2021 recommendations as to when to offer IUI as it was noted from the retrospective medical record review 4 couples were offered IUI treatment modality despite having bilaterally blocked tubes and about 52 couples were offered IUI while having suboptimal TMSC below 5 million and below 1 million. These findings suggest additional fertility-limiting factors, other than sperm count—such as sperm DNA integrity, subclinical tubal dysfunction, advanced maternal age, or prolonged infertility duration—might have played a role.

Contrasting with findings supporting IUI as a first-line treatment for mild male factor infertility (60), our study in a setting with a high prevalence of severe abnormalities found a modest IUI success rate (7.7%) that was significantly lower than ICSI (19.0%). Crucially, semen parameters were not an independent predictor of success. This suggests that a universal IUI-first approach is

suboptimal; treatment triage should instead be based on a broader clinical assessment beyond semen analysis alone.

Multivariable analysis from our study and prior work by Yu et al. (50) indicates that female age, BMI, duration of infertility, and TMSC are key determinants of IUI success. The generally low IUI pregnancy rate therefore may emphasize the need for refined triage criteria in Ethiopia, especially for couples with tubal disease or older female partner age and also when male partners have semen parameters outside the updated WHO reference ranges.

6.5. ICSI Outcomes and the Central Role of Assisted Micromanipulation

In this study ICSI was more commonly used for couples with abnormal semen analysis in 62.5% of cases out of 557 couples reflecting clinical prioritization and preferential use of it in male factor infertility. Contrary to international recommendation and guidelines including our country, quite a large proportion of couples (37.5%; 209 out of 557) without clear male factor indication underwent ICSI for their first ART attempt though ICSI has no clear medical benefit over Conventional IVF it should be reserved for confirmed male factor infertility (10,26,61). In the preset study there was on over use of ICSI for non-male factor infertility cases with increased cost to the couples may be due to fear of fertilization failure.

ICSI yielded biochemical pregnancy rate of 25.5% and a clinical pregnancy rate of 19.0%, consistent with findings from comparable low-resource settings where rates range between 18–28% per cycle. Nigerian multicenter ART data reported 22%, Indian tertiary centers reported 25%, and private Ethiopian clinics have documented 26.6% in recent years. The fertilization rate of 69.6% reflects competent laboratory performance and mirrors global benchmarks.

Importantly, after statistical adjustment, semen abnormality was not an independent predictor of clinical pregnancy. This is consistent with current literature showing that once ICSI is employed, traditional semen parameters lose prognostic significance because the technique effectively bypasses concentration, motility, and morphology defects. Instead, female age and treatment modality were strong predictors of outcome, consistent with global ART evidence (3,26.48).

The utilization of surgical sperm retrieval (TESE) in 9.0% of ICSI cycles for azoospermia demonstrates that Ethiopian ART centers can successfully manage advanced male factor infertility using internationally accepted approaches (33,34,43).

Our key findings from this study may indicate that the ICSI procedure itself may mitigate the impact of basic semen abnormalities on early embryogenesis, with many studies including our study which has similar finding and are in agreement with studies (52,53) reporting minimal association between these parameters and blastocyst quality or morphology. Instead, evidence is converging on the higher importance of embryo-related factors in determining early pregnancy outcomes. Specifically, the quality of the blastocyst's inner cell mass (ICM) has been identified as a critical and more reliable predictor of biochemical pregnancy and initial implantation success than paternal characteristics or standard semen analysis. (52,53)

Although male factors are essential to achieving fertilization, their role may be superseded by embryo morphology particularly the inner cell mass. Growing number of evidences from many research suggests a critical distinction between the impact of sperm and oocyte/embryo morphology. These findings highlight the importance of future well designed further research in Ethiopian setting to better understand the distinct role of sperm quality on embryo development in assisted reproductive technology outcomes.

6.6. Comparative Effectiveness: ICSI vs IUI

In this study about two to three times more clinical pregnancy rate is observed with ICSI treatment modality compared to IUI which reflects well-established clinical evidence. It is a well-established fact that IUI has limited benefit in moderate and severe male factor infertility and when combined etiologies co-exist (3,24). The discrepancy in this study clearly shows sub optimal allocation of infertile couples in this setting. Fifty-five percent of couples underwent IUI including some with conditions like tubal factor, advanced female age and lower TMSCs where success is basically and inherently known to be low. Therefore, findings from the present research in our study support the importance of more selected patient triage directing high risk infertile couples such as: severe male factor, tubal pathology, or older female age groups toward IVF/ICSI instead of time taking, prolonged and futile IUI attempts.

The overall clinical pregnancy rate of 12.8% per initiated treatment cycle from our study is lower than findings from high-resource settings but it is comparable and in agreement with outcomes from resource-constrained African fertility centers (35,39). The substantial difference between IUI (approximately 8%) and IVF-ICSI (approximately 20%) success rates corroborates international evidence that IUI has limited efficacy in moderate-to-severe male factor infertility (3,24).

Remarkably, after multivariable adjustment, abnormal semen parameters were not independently associated with clinical pregnancy in our study. This finding is in agreement with recent large cohort studies demonstrating that once ICSI is employed, conventional semen parameters lose prognostic significance because the technique directly overcomes defects in concentration, motility, and morphology (48). Instead, female age ≥35 years and treatment modality type emerged as the strongest predictors, reinforcing the well-documented dominance of female age and the effectiveness of ICSI in bypassing sperm-related barriers (3,26,48,59).

The absence of an independent effect of semen parameter abnormalities in the final model should not be interpreted as male factor being irrelevant; rather, it highlights the success of current ART in overcoming most sperm defects when appropriately applied. In a setting where severe male factor is prevalent, this findings from the present research even though it is single cycle treatment, might support current AUA/ASRM guidelines recommending early progression to ICSI rather than multiple IUI cycles (3,26,59) and suggests that prolonged IUI attempts in severe cases may represent inefficient use of limited resources.

6.7. Female Factor Infertility and Treatment Selection

In the present study female factor accounted for large majority of infertile couple (45.7%) out of which tubal factor accounted for 25.0% of women and this finding was consistent with most regional data suggesting a high prevalence of pelvic infection in sub-Saharan Africa regions. Quite a large proportion of these infertile couples underwent IUI treatment modality, which essentially is ineffective for tubal diseases, likely contributing to the lower IUI group clinical pregnancy success rate. This mismatch between treatment and pathology warrants the need for

structured triage pathways in line with WHO 2021 recommendation and the national fertility prevention and care implementation guidelines (15,59,61)

Although this study mainly focused on male abnormalities, female factors were found to have significant influence on clinical pregnancies. Clinical pregnancy rates were higher among infertile couples where the female partners age was ≤30 years and progressively declined with age. These findings are in consistent agreement with established age-related reductions in fecundity (5,26). Hence, women with tubal factor infertility, diminished ovarian reserve or age ≥35 years would benefit more from fast track to timely and early IVF/ICSI, which bypass tubal disease and mitigate age-related fertility decline.

This study provides the first comprehensive and locally relevant evidence on the interaction between semen parameters and ART outcomes in Ethiopian setting. Its key, counterintuitive finding is that while severe semen abnormalities are highly prevalent, they are not the primary determinant of treatment success rather, clinical pregnancy outcomes are predominantly shaped by female age and the selection of ICSI over IUI. This necessitates a fundamental shift in clinical paradigm from a semen-centric view of male infertility to an integrated, couple-based model for appropriate patient selection and treatment triage.

Consequently, the critical and main challenge for Ethiopian ART programs is no longer simply adopting ICSI, but defining the precise clinical criteria that should guide ICSI use over less invasive options like IUI and IVF, meanwhile confronting systemic barriers like patient dropout that undermine the accurate measurement of success in ART.

7. Strength and limitation of the study

7.1. Strengths

This study's extensive dataset, which includes consecutive treatment cycles gathered over a four-year period from two significant private fertility institutions, sets it apart as the largest cohort of infertile couples (n = 1,242) evaluated in Addis Ababa, Ethiopia to date. The study increases the representativeness of findings in the context of private fertility care and achieves significant statistical power. In a setting where there is still a dearth of research on infertility, our multicenter strategy increases the data' external validity and offers solid, locally created evidence.

In order to ensure worldwide comparability, the study used the WHO 2021 standardized diagnostic criteria. The use of multivariable binary logistic regression was crucial in determining that semen parameters were not independent predictors of clinical pregnancy in ART success because it made it possible to identify independent predictors of success while accounting for potential confounders.

A thorough, comparative analysis was made possible by the two-arm inclusion of both IUI and ICSI treatment methods. Additionally, the study offers a comprehensive and clinically significant evaluation of ART success determinants in Ethiopia by simultaneously evaluating male and female factors and differentiating biochemical from clinical pregnancy.

7.2. Limitations

A number of limitations inherent in the retrospective chart-review approach of this study should be taken into consideration when interpreting the results. A number of potentially significant confounders, including comprehensive hormone profiles, endometrial thickness, and body mass index for both couples, were missing due to incomplete reporting. Additionally, it was not possible to properly evaluate the role of important male-factor characteristics to pregnancy outcomes, such as sperm DNA fragmentation, genetic test findings, and an assessment of seminal oxidative stress test.

The study's biggest drawback relates to outcome measurement. Due to significant loss to follow-up, data on continued pregnancy at 12 weeks and live birth were not consistently available, hence the primary outcome was limited to clinical pregnancy. This means that the study's conclusions are limited to clinical pregnancy, which is an earlier and less definite outcome, and prevents the computation of cumulative live birth rates, which are the definitive metrics of ART efficacy generally.

Lastly, the study was done on a cycle-by-cycle basis (initial cycle only), which would not accurately represent cumulative success over several treatments. The results have limited applicability to Ethiopian rural communities and public healthcare settings because the study was only carried out in private facilities in Addis Ababa. As a result, bigger, prospective multi-center studies are needed for external validation of the results.

8. CONCLUSION AND RECOMMENDATION

8.1. Conclusion

More than half of men seeking treatment at major private fertility centers in Addis Ababa present with at least one abnormal semen parameter, confirming a significant burden of potential male factor infertility. This study offers a thorough analysis of infertility treatment outcomes in Ethiopia. This study shows that among men seeking infertility treatment in Addis Ababa, semen characteristics below the WHO 2021 5th percentile are more common, accounting for 55.6% of the 1242 infertile couples. However, these factors did not independently predict clinical pregnancy after first-cycle ART treatments; instead, the use of ICSI versus IUI treatment modality and female age were the main predictors of success.

The study's conclusions cast doubt on the widely held belief that ICSI's ability to overcome male factor infertility is the only reason for the increased clinical pregnancy. The apparent superiority of ICSI may be attributed to other, unmeasured factors associated with the choice of treatment technique, as suggested by the lack of predictive value for semen parameters. A crucial confusion for routine clinical practice arises because, although ICSI seems to be more effective, the criteria for selecting it over less invasive and less expensive IUI are still unclear. Furthermore, the measurement of clinically significant outcomes such as the live birth rate and continued pregnancy rate is severely limited by the high rate of loss to follow-up.

Therefore, while these results demonstrate the feasibility of providing ART in this setting, they primarily highlight an urgent need for two actions: Improved follow-up systems to measure true success rates, and Prospective research to identify the multifactorial predictors that can rationally guide the choice between IUI and ICSI, optimizing outcomes and resource use.

8.2. Recommendation

The following recommendations are proposed based on the findings of this study on the prevalence of abnormal semen parameters and their treatment outcomes following first-cycle IUI and ICSI.

A. **Recommendations for Clinical Practice:**

1. **Integration of Semen Analysis into Holistic Assessment of the couples**:

When applying WHO 2021 semen parameter categories in daily clinical routine, clinicians should not use the numerical values in isolation to predict IUI or ICSI success or to select treatment modalities. Abnormal semen parameters alone are not a reliable bad prognostic indicator for ART success in this setting. Semen analysis reports should be interpreted as one component within a comprehensive diagnostic evaluation and management of both partners.

2. **Optimizing Treatment Selection and triage of infertile couple with abnormal semen parameters:**

The selection between ICSI and IUI should be based on a multifactorial assessment including, but not limited to, duration of infertility, female age, ovarian reserve, tubal patency, and previous cycle history, instead of semen parameters alone as per WHO, ASRM AUA guideline.

B. **Recommendations for IVF centers on Data Management:**

3. **Implementation of Standardized Follow-up Protocols**:

IVF centers should strengthen their data systems to ensure standardized and complete documentation of each treatment cycle outcomes, including tracking of ongoing pregnancy and live birth rates. This is important for accurate quality assurance and conducting future research.

C. **Recommendations for Future Research:**

4. Further studies are required to investigate lifestyle, environmental, infectious and systemic factors causing and contributing to this phenomenon of higher prevalence of abnormal semen

parameters cases among Ethiopian infertile couples, which could improve future interventions in infertile couple`s care and treatments.

5. Conduct Prospective, Multifactorial Studies population based studies:

Future research should employ well-designed prospective cohorts to identify the key predictors of ART success in Ethiopia. These studies must collect comprehensive data across private and public IVF centers on female factors, stimulation protocols, embryology data, and longitudinal outcomes.

6. **Compare Treatment Pathways for guiding rational selection between IUI and ICSI:**

A prospective comparative multi centered study is needed to rigorously evaluate under what specific clinical circumstances IUI versus ICSI provides the optimal benefit at couple level, moving beyond semen-based decision-making.

Therefore, since this is a retrospective study, we suggest a prospective comparative study to be done in the future for better recommendation.

9. REFERENCES

1. Zegers-Hochschild F AG, De Mouzon J, Ishihara O, Mansour R, Nygren K, et al. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology. Fertil Steril. 2009; 92:1520-4.

2. Hull MG GC, Kelly NJ, Conway DI, Foster PA, Hinton RA et al. Population study of causes, treatment, and outcome of infertility. Br Med J (Clin Res Ed). 1985; 291:1693-7.

3. Peter N. Schlegel MD, et al. Diagnosis and treatment of infertility in men. AUA/ASRM guideline part. 2021; 115:54-61

4. Mascarenhas MN FS, Boerma T, Vanderpoel S, Stevens GA. National, Regional, and Global Trends in Infertility Prevalence since 1990: A Systematic Analysis of 277 Health Surveys. PLoS Medicine. 2012;9(e1001356):12.

5. Chandra A CC, Stephen EH. Infertility and Impaired Fecundity in the United States, 1982–2010: Data from the National Survey of Family Growth. national Center for Health Statistics: Hyattsville, MD. 2013.

6. Oakley L DP, Maconochie N. Lifetime prevalence of infertility and infertility treatment in the UK: results from a population-based survey of reproduction. Human Reproduction. 2008;23(2):447-50.

7. Adetoro OO EE. The prevalence of infertility in a rural Nigerian community. African Journal of Medicine and Medical Sciences. 1991; 20:23-7.

8. Okonofua FE HD, Odebiyi A, Thomas K, Snow RC. The social meaning of infertility in Southwest Nigeria. Health Transition Review. 1997; 7:205-20.

9. Legese N TA, Roba KT, Demeke H. The prevalence of infertility and factors associated with infertility in Ethiopia: Analysis of Ethiopian Demographic and Health Survey (EDHS). PLoS ONE. 2023;18(10).

10. Peter AO TA, Olufemi AP, et al. Pattern of semen parameters and factors associated with infertility in male partners of infertile couples in Nigeria. Andrology. 2016;5(1):1-7.

11. Li WN JM, Peng YQ, et al. Semen quality pattern and age threshold: a retrospective cross-sectional study of 71,623 infertile men in China, between 2011 and 2017. Reprod Biol Endocrinol 2019(17):107.

12. Kurdukar MD PA, Pandit GA, et al. Patterns of semen analysis in infertile couples at the tertiary care center. Int J Curr Res. 2016;8(10):40704–7.

13. Ugwuja EI UN, Ejikeme BN. Prevalence of low sperm count and abnormal semen parameters in male partners of women consulting at infertility clinic in Abakaliki, Nigeria. Afr J Reprod Health. 2008;12(1):67-72.

14. GR D. Inflammatory associated obstruction of the male reproductive tract. Andrologia 2003;35(5):321-4.

15. Organization. WH. WHO laboratory manual for the examination and processing of human semen. 2021.

16. Cohlen BJ. Intrauterine insemination: continuing role in modern fertility care. Gynecol Endocrinol. 2020;36(4):285–289.

17. Bernie AM, Mata DA, Ramasamy R, Schlegel PN. Outcomes of microdissection versus conventional testicular sperm extraction. Fertil Steril. 2015;104(6):1393–1399.

18. Ramya C RI, Premalatha P, et al. Patterns of semen analysis in male partners of infertile couples at a tertiary care hospital. Indian J Pathol Oncol. 2017;4(4):536-9.

19. Agarwal A MA, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reprod Biol Endocrinol. 2015; 13:37.

20. Cannarella R GM, Rambhatla A, Agarwal A. Temporal decline of sperm concentration: role of endocrine disruptors. Endocrine. 2023; 79:1-16.

21. Sermondade N ea. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Human Reproduction Update. 2013;19(3):221-31.

22. Rambhatla A, Shah, R., Pinggera, G. M., Mostafa, T., Atmoko, W., Saleh, R., et al. Pharmacological therapies for male infertility. Pharmacol. 2024;77(100017).

23. Kim HJ, Seo, J. T., Kim, K. J., Ahn, H., Jeong, J. Y., Kim, J. H., et al. Clinical significance of subclinical varicocelectomy in male infertility: systematic review and meta-analysis. Andrologia. 2016;48(6):654-61.

24. Sharma AP, Sharma, G., and Kumar, R. Systematic review and metaanalysis on effect of carnitine, coenzyme Q10 and selenium on pregnancy and semen parameters in couples with idiopathic male infertility. Urology. 2022; 161:4-11

25. Biradar, K. D. (2017). Male factor in infertility: study from a tertiary care hospital. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 5(6), 2022–2025. https://doi.org/10.18203/2320-1770.ijrcog20161710

26. Schlegel PNS, M.; Collura, B.; De Jonge, C.J.; Eisenberg, M.L.; Lamb, D.J.; Mulhall, J.P.; Niederberger, C.; Sandlow, J.I.;Sokol, R.Z.; et al. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I. Fertil Steri. 2021; 115:54-61.

27. Sorena K CJ, Zhang C. Impacts of abstinence time on semen parameters in a large population-based cohort of subfertile men. Urology. 2017; 108:90-5.

28. Mahdi MA SD, Almhmdi NA. Evaluation of the impact of the level of (Testosterone, Luteinizing Hormone, Follicle-Stimulating Hormone and Prolactin) on some semen parameters in infertile males. Tikrit Journal of Pure Science. 2018;23(7).

29. Veleva L MT, Bochev I. Relationship of somatic indicators with motility and velocity parameters of sperm movement. Reproductive Health. 2015; 22:9-13.

30. Rusz A PA, Wagenlehner F, et al. Influence of urogenital infections and inflammation on semen quality and male fertility. The World Journal of Urology. 2012;30(1):23-30.

31. Barratt CLRB, L.; De Jonge, C.J.; Lamb, D.J.; Martini, F.O.; McLachlan, R.; Oates, R.D.; Van Der Poel, S.; John, B.S.;Sigman, M.; et al. The diagnosis of male infertility: An analysis of

the evidence to support the development of global WHO guidance—Challenges and future research opportunities. Hum Reprod Update. 2017; 23:660-80.

32. Sikka SC HW. Current updates on laboratory techniques for the diagnosis of male reproductive failure. Asian Journal of Andrology. 2016; 18:392-401.

33. Practice Committee of the American Society for Reproductive Medicine in collaboration with the Society for Male Reproduction and Urology. Evaluation of the azoospermic male: a committee opinion. Fertil Steril. 2018 May;109(5):777-782

34. Baker K SEJ. Obstructive azoospermia: reconstructive techniques and results. Clinics (Sao Paulo. 2013; 68:61-73.

35. Adeniji RA OO, Okunlola MA, Aimakhu CO. Pattern of semen analysis of male partners of infertile couples at the University College Hospital, Ibadan. W Afr J Med. 2003;22(3):243-9.

36. Baoyi Huang ZW, Yanxiang Kong, Mengqi Jin and Lin Ma. Global, regional and national burden of male infertility in 204 countries and territories between 1990 and 2019: an analysis of global burden of disease study. BMC Public Health. 2023;23(2195).

37. Melese Shenkut Abebe MAaYA. Primary and secondary infertility in Africa: systematic review with meta-analysis. Fertility Research and Practice. 2020;6(20).

38. Matthew Igwe Nwali JA. Reports of Semen Parameters Among Male Partners of Infertile Couple Presenting at the Gynecological Clinic of A Tertiary Hospital Southeast, Nigeria. International Journal of Health Sciences. 2023;11(2):18-24.

39. Tilahun T, Oljira R, Getahun A. Pattern of semen analysis in male partners of infertile couples in Western Ethiopia: Retrospective cross-sectional study. Sage Open Medicine. 2022;10. doi:10.1177/20503121221088100

40. Christian O. Igibah JO, Simeon C. Amadi, Theophilus N. Ilenbodiaye, Francis Erah, Ada N. Okocha, Mkpe Abbey, Paul L. Kua, Chidiebere N. Ononuju, Oluwagbemiga Adewale. Abnormalities of semen parameters among male partners of infertile couples in a sub-urban tertiary hospital in Nigeria. Int J Reprod Contracept Obstet Gynecol. 2023;12(10):2900-5.

41. Legese N TA, Roba KT, Demeke H. The prevalence of infertility and factors associated with infertility in Ethiopia: Analysis of Ethiopian Demographic and Health Survey (EDHS). PLoS ONE. 2023;18(10).

42. Akash More BRS, Deepti Shrivastava, Ujwal Gajbe, Nandkishor Bankar. . A Study of Semen Parameter Contributing Infertility in Vidarbha Region. Indian Journal of Forensic Medicine & Toxicology. 2020;14(4).

43. Saleh I, Getachew S, Kedir M, Sheikh AM. Trend analysis of frozen embryo transfer at Alhikmah Fertility Center, Addis Ababa, Ethiopia. Ethiop J Reprod Health. 2023 Jan;15(1):47.

44. Tsegazeab H. Prevalence of male factor infertility and associated factors in couples seeking fertility care at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia [Unpublished specialty thesis]. Addis Ababa: St. Paul's Hospital Millennium Medical College; 2021.https://repo.sphmmc.edu.et/handle/123456789/69

45. Ventimiglia E, Ippolito, S., Capogrosso, P., Penderzoli, F., Cazzaniga, W., Cavarretta, Salonia. Primary, secondary and compensated hypogonadism: A novel risk stratification for infertile men. Andrology. 2017; 5:505-10.

46. Shoshany O, Abhyankar, N., Mufarreh, N., Daniel, G., & Niederberger, C. Outcomes of anastrozole in oligozoospermic hypoandro-genic subfertile men. Fertility and Sterility, 1. 2017;107:589-94.

47. Sermondade N FC, Fezeu L, et al. BMI in relation to sperm count: An updated systematic review and collaborative meta-analysis. Human Reproduction Update. 2013;19(3):221-31.

48. Xin Ye TP, Zhicong Chen, Chen Liao, Xiaomin Li, Yu Lan, Xin Fu, Geng An. Semen parameters' mediation effect on the association between advanced paternal age and IVF clinical outcomes: A 10-year retrospective cohort study. Maturitas. 2023; 173:20-7.

49. Wardah Alasmari FE, Zainab Albar, Abdulrahim Gari, Mamdoh Eskandar, Mohammed Al Fageah, Shamsuldin Zawawi. High Proportion of Abnormal Semen Characteristics among Saudi Infertile Couples. Clinical Medicine and Diagnostics. 2018;8(1):14-20.

50. Chunmei- Yu L-B, Jian mei-Zhou, Xiao yu-Wang, Li Chen and Jinghua- Zhang. . Analysis of factors associated with IUI pregnancy outcomes in elderly and young patients. BMC Women's Health. 2024;24(28).

51. Kasman AM, Li S, Zhao Q, Behr B, Eisenberg ML. Relationship between male age, semen parameters and assisted reproductive technology outcomes. Andrology. 2021 Jan;9(1):245-252. doi: 10.1111/andr.12908. Epub 2020 Oct 8. PMID: 32964702.

52. Pande DB, Deshmukh H, Bhadauria S, Tomar GS. Impact of Male Age and Semen Parameters on Blastocyst Morphology, Beta-HCG Positivity and Pregnancy Viability: A Retrospective Analysis in Frozen Embryo Transfer Cycles. J Obstet Gynaecol India. 2025 Jun;75(3):206-212. doi: 10.1007/s13224-024-02079-0. Epub 2025 Jan 22. PMID: 40584805; PMCID: PMC12204959.

53. Shanthi DT, Gopinath P, Kumar KD, Iyer RP, Kesavaramanujam R, Karunakaran GK. Evaluating the Contribution of Oocyte, Sperm, and Uterus in Determining the Outcome of Intracytoplasmic Sperm Injection - A Retrospective Observational Comparative Study on Intracytoplasmic Sperm Injection using Own Oocytes and Donor Oocytes. J Hum Reprod Sci. 2021 Jul-Sep;14(3):281-287. doi: 10.4103/jhrs.jhrs_20_21. Epub 2021 Sep 28. PMID: 34759618; PMCID: PMC8527072.

54. Boeri L, Fallara G, Pozzi E, et al. The impact of different WHO reference criteria for semen analysis in clinical practice: Who will benefit from the new 2021 thresholds for normal semen parameters? Andrology. 2022; 10:1134–1142. https://doi.org/10.1111/andr.13213

55. Umar AG, Panti, A.A., Mbakwe, M., Ahmed, Y., Garba, J.A. and Nnadi, D.C. (2020) The Pattern of Seminal Fluid Analysis among Male Partners Attending an Infertility Clinic in a Nigerian Tertiary Health Institution. pen Journal of Obstetrics and Gynecology. 2020; 10:957-67.

56. Dr.E.Hariharan DSE, Dr.K.Jayashree Srinivasan. Study On Pattern of Abnormal Semen Parameters Among Male Partners of Infertile Couples Attending Fertility Centre in A Tertiary Care Referral Hospital. European Journal of Molecular & Clinical Medicine. 2020;7(8).

57. Cui F ZYaFY. Adjuvant treatment with Wu-Zi-Yan-Zong formula for abnormal sperm parameters associated with male infertility: a meta-analysis of randomized controlled trials. Front Pharmacol 2025;16(1580705).

58. Prabhavathi C. PR, Vadakaluru Uthpala. Prevalence of Abnormal Semen Analysis in Patients of Infertility in a Tertiary Care Hospital. International Journal of Pharmaceutical and Clinical Research. 2022;14(11):459-62.

59. Boitrelle FS, R.;Saleh, R.; Henkel, R.; Kandil, H.;Chung, E.; Vogiatzi, P.; Zini, A.; Arafa, M.; Agarwal, A. The Sixth Edition of the WHO Manual for Human Semen Analysis: A Critical Review and SWOT Analysis. WHO. 2021;11(1368).

60. Amanullah M, Ahsan MA, Akram MS, Arefin MS, Hasan F, Tabassum S. Effectiveness of Intrauterine Insemination in Unexplained Infertility and Male Subfertility with Mild Form of Oligo Asthenoteratozoospermia. Am J Appl Sci Res. 2022;8(4):99-106. doi: 10.11648/j.ajasr.20220804.15

61. Ministry of Health, Ethiopia. National infertility prevention and care implementation guideline. Federal Democratic Republic of Ethiopia; 2025 Aug.

ANNEXS

Annex I: Data abstraction form

INFERTILITY STUDY DATA COLLECTION TOOL

Study Title: Prevalence, patterns and Treatment Outcomes in Infertile Couples with Abnormal Semen Parameters: A Retrospective Cross sectional Study on Semen Analysis, IUI, and ICSI Outcomes

SECTION 1: DEMOGRAPHIC & CLINICAL INFORMATION

1. Patient ID: _____
2. Date IUI/ICSI in year: //_____
3. Center/Clinic:
   ☐ St. Paul's MMC ☐ AL-HIKMAH ☐ ETHIO-FERTILITY ☐ New Leaf
4. Male Age: _____ years
5. Female Age: _____ years
6. Duration of Infertility: _____ years
7. Type of Infertility: ☐ Primary ☐ Secondary
8. Marital Status: ☐ Married ☐ Cohabiting ☐ Other: _____
9. Duration of marriage: _____ years
10. Male BMI (kg/m²): _____
11. Female BMI (kg/m²): _____

SECTION 2: SEMEN ANALYSIS (WHO 2021 CRITERIA)

12. Days of Abstinence: _____ (Ideal 2–7)

13. Semen Volume (mL): _____

14. Sperm Concentration (million/mL): _____

15. Total Motility (%): _____

16. Progressive Motility (%): _____

17. Morphology (Strict, % normal forms): _____

18. Vitality (% live sperm): _____

19. Azoospermia: ☐ Yes ☐ No

20. Leukocytospermia: ☐ Present ☐ Absent

21. Abnormal Pattern: Semen Abnormality Classification
    ☐Normal ☐Azospermia ☐Oligozoospermia ☐Asthenozoospermia ☐Teratozoospermia ☐Combination OAT

SECTION 3: REPRODUCTIVE AND MEDICAL HISTORY FOR FEMALE PARTNER

22. Previous Pregnancy (female): ☐ Yes ☐ No → If yes, how many? _____
23. Previous Live Births: ☐ Yes ☐ No

24. History of Miscarriage or Abortion: ☐ Yes ☐ No

25. History of Stillbirth: ☐ Yes ☐ No

26. History of Ectopic Pregnancy: ☐ Yes ☐ No

27. Female Menstrual Cycle: ☐ Regular ☐ Irregular

28. PID or Pelvic Infection (Female): ☐ Yes ☐ No

29. Chronic illness female partner

☐ Diabetes ☐ Hypertension ☐ None ☐ Other: _____

30. History of pelvic Surgery – Female: ☐ Yes ☐ No

31. Infertility Diagnosis (select all that apply):

☐ Tubal Factor ☐ PCOS ☐ Endometriosis ☐ Uterine ☐ Unexplained ☐ Other: _____

32. AMH Level (ng/mL): _____

33. Antral Follicle Count (AFC): _____

34. Endometrial Thickness before treatment (mm): _____

35. Tubal Patency (HSG/SIS):

☐ Bilateral Patent ☐ Unilateral Block ☐ Bilateral Block

SECTION 4: MEDICAL & LIFESTYLE HISTORY FOR MALE PARTNER

36. History of Surgery – Male: ☐ Yes ☐ No

37. History of Varicocele (Male): ☐ Yes ☐ No

38. History of Orchitis /swelling / trauma testicular (Male): ☐ Yes ☐ No

39. Previous Fertility Treatment: ☐ Yes ☐ No

If Yes, type: ☐ IUI ☐ IVF ☐ ICSI ☐ Other: _____

40. Male Smoking: ☐ Yes ☐ No

41. Male Alcohol Use: ☐ Yes ☐ No

42. Male Khat Use: ☐ Yes ☐ No

43. Chronic Illness (male Partner):

☐ Diabetes ☐ Hypertension ☐ None ☐ Other: _____

SECTION 5: FERTILITY TREATMENT OPTIONS PROVIDED FOR THE COUPLE

44. ART Type Used:

☐ Intrauterine Insemination (IUI)

☐ Conventional IVF

☐ ICSI

☐ Not yet treated

(Skip to Section 6 if IUI, or Section 7 if IVF/ICSI)

SECTION 6: FIRST CYCLE IUI TREATMENT DETAILS INCLUDING OUTCOMES (IF APPLICABLE)

45. Cycle Type: ☐ Natural ☐ Stimulated
46. Stimulation Protocol: Drug used

☐ Clomiphene ☐ Letrozole ☐ Gonadotropins ☐ Combined

47. TMSC (post-wash): _____ million
48. No. of Dominant Follicles (>14 mm): _____
49. Endometrial Thickness at the time of Triger: _____ mm
50. Insemination Timing Post-HCG:

☐ 12 hr ☐ 24 hr ☐ 36 hr

51. Outcome of IUI:

☐ Chemical Pregnancy (positive urine/β-HCG)

☐ Clinical Pregnancy (US-confirmed sac)

☐ No pregnancy

52. Final Pregnancy Outcome:

☐ Live Birth ☐ Miscarriage (<28weeks) ☐ Ongoing ☐ Ectopic

SECTION 7: FIRST CYCLE IVF WITH ICSI TREATMENT DETAILS INCLUING OUTCOMES (IF APPLICABLE)

53. Type of ART:

☐ Conventional IVF ☐ ICSI

54. Sperm Source:

☐ Ejaculate ☐ TESE ☐ Micro-TESE

55. Stimulation Protocol:

☐ GnRH Antagonist

☐ GnRH Agonist

☐ Minimal Stimulation

☐ Progestin-Primed Ovarian Stimulation (PPOS)

56. Total Oocytes Retrieved: _____

57. Mature Oocytes (MII): _____

58. Fertilization Rate: _____ %

59. Embryo Quality:

Day 3: ☐ Grade 1 ☐ Grade 2 ☐ Grade 3

Day 5: ☐ Good ☐ Fair ☐ Poor

60. Embryos Transferred: ☐ ET ☐ FET

61. Embryos Transferred): _____

62. Endometrial Thickness at Transfer: _____ mm

63. Outcome of IVF/ICSI:

☐ Chemical Pregnancy (urine or β-HCG)

☐ Clinical Pregnancy (gestational sac seen 6/7 week)

☐ No pregnancy

64. Final Pregnancy Outcome:

☐ Live Birth ☐ Miscarriage ☐ Ongoing ☐ Ectopic

65. Type of Pregnancy:

☐ Singleton ☐ Twin ☐ Triplet

SECTION 8: OPTIONAL DELIVERY & NEONATAL OUTCOME (IF PREGNANT AND DATA AVAILABLE ON PATIENT MEDICAL RECORD)

66. Birth Weight: _____ grams
67. Gestational Age at Delivery: _____ weeks

68. Sex/s of delivered babies

☐ Male ☐ female

69. Any Pregnancy Complications documented on the patient medical chart

☐ None ☐ GDM ☐ Preeclampsia ☐ Other: _____

70. Where was the delivery?

☐ Addis Ababa ☐ outside Addis Ababa ☐ outside Ethiopia

SECTION 9: Data Entry Info

Data Collector Name: _____

Signature: _____

Date of Entry: //_____

Comments: _____

Annex II: Waiver of Consent Request

From: Dr. Nuredin Awel Mohammed
Date: 8/22/2025 G.C

To: Chair, Departmental Research and Publication Committee (DRPC)
Addis Ababa University, College of Health Sciences, School of Medicine
Department of Obstetrics and Gynecology

Subject: Waiver of Informed Consent – Retrospective Record Review

Dear Chair,

I request a waiver of informed consent for my study titled:
"Prevalence, Patterns, and Treatment Outcomes of Abnormal Semen Parameters Among Infertile Couples in Ethiopia: A Three-Year Retrospective Study", undertaken as part of the Subspecialty Program in Reproductive Endocrinology and Infertility at Addis Ababa University. The study will involve retrospective review of existing clinical records from selected fertility centers in Addis Ababa.

Justifications for Waiver:

1. **Minimal Risk** – Only pre-defined information from routine, clinically indicated procedures will be collected. The main potential risk (breach of confidentiality) will be mitigated through complete anonymization, encryption, and separation of identifiers from study data. No personal identifiers will be entered into the Kobo Collect database.
2. **No Adverse Effect on Rights or Welfare** – All procedures were completed before the study. Findings will be analyzed in aggregate and will not influence any patient's clinical care.
3. **Practicability** – Contacting all eligible patients from a three-year period would be logistically and financially impractical and could itself constitute a privacy breach.

4. **Confidentiality and Security** – A temporary code–identifier list (for duplicate checks) will be stored separately in a password-protected, encrypted file accessible only to the principal investigator, and destroyed after data cleaning. Electronic data will be stored on a password-protected computer and backed up on an encrypted device; paper notes, if any, will be locked and destroyed after use.

Considering the retrospective nature of the study with its minimal risk, I kindly request a waiver of informed consent to be approved by the DRPC.

Sincerely,

Dr. Nuredin Awel Mohammed
OB-GYN Specialist, REI Fellow
AAU, CHS, SOM Department of Obstetrics and Gynecology
Phone: +251 911 393 614
Email: nuredinawel@gmail.com