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DIAGNOSIS AND MANAGEMENT OF INFERTILITY: A PRACTICAL CLINICAL REVIEW

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ABSTRACT

Background: Infertility, defined as the failure to achieve pregnancy after 12 months of regular unprotected intercourse, affects a substantial proportion of reproductive-age couples and is associated with psychological and social burden.

Objective: To outline a structured, evidence-based approach to the diagnosis and management of infertility with a focus on age-stratified, resource-sensitive algorithms.

Methods: Narrative review of recent guidelines and systematic reviews on infertility diagnosis and treatment published between 2015 and 2024, identified via PubMed and guideline repositories of the American Society for Reproductive Medicine (ASRM) and World Health Organization (WHO).

Results: Common etiologies include ovulatory dysfunction, male factor infertility, tubal disease, endometriosis, and unexplained infertility. Initial evaluation should include history, physical examination, ovulation assessment, semen analysis, and tubal/uterine imaging when indicated.

First-line treatments include ovulation induction with letrozole for anovulatory women, intrauterine insemination (IUI) for mild male factor or unexplained infertility, and in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI) for bilateral tubal factor, severe male factor, or women of advanced reproductive age.

Conclusion: A stepwise, age-appropriated management algorithm can optimize pregnancy outcomes and help clinicians avoid unnecessary delays to effective treatment.

KEYWORDS: Infertility; diagnosis; management; algorithm; ovulation induction; assisted reproductive technology; IVF

INTRODUCTION

Infertility is classically defined as the inability to achieve pregnancy after 12 months of regular unprotected intercourse among couples of reproductive age[1,2]. In the United States, approximately 12.7% of women aged 15–49 years seek infertility services each year, and similar or higher prevalence is reported in many low- and middle-income countries, including India[1,6]. The diagnosis of infertility is often stressful for couples, and early, systematic evaluation is essential to reduce delay and maximize the likelihood of successful conception[7,8].

Common etiologic categories include ovulatory dysfunction, male factor infertility, tubal disease, endometriosis, uterine pathology, diminished ovarian reserve, and unexplained infertility[3,6].

Ovulatory disorders alone account for about one-quarter of infertility diagnoses, with polycystic ovary syndrome (PCOS) being the most frequent cause of anovulation[3,6]. Male factor and tubal disease are also major contributors, while approximately 15% of infertile couples are labeled as having unexplained infertility after standard evaluation.visualize[3,6].

Recent guidelines from the WHO and professional societies emphasize parallel evaluation of both partners, cost-effective and expedient diagnostics, and individualized treatment based on age, duration of infertility, ovarian reserve, and resource availability[5,4,9]. However, most evidence on stepwise management and outcome prediction is derived from high-income settings, and

context-specific algorithms for low- and middle-income countries remain limited4,7].

The aim of this article is to synthesize current evidence into a practical, age-stratified algorithm for the diagnosis and management of infertility suitable for both urban and tertiary-care settings. We focus on **diagnostic pathways, first-line medical and surgical options, and the appropriate timing of assisted reproductive technologies (ART) such as IUI and IVF-ICSI [3,1].**

METHODS

This article is based on a **narrative review** of recent guidelines and systematic reviews on infertility diagnosis and management[3,4]. We searched PubMed and guideline repositories (including WHO-IRIS, ASRM, and ESHRE resources) for English-language articles published between January 2015 and December 2024 using the key terms *infertility, diagnosis, management, ovulation induction, intrauterine insemination, IVF, ICSI, and guidelines[3,5].*

Articles included were randomized clinical trials (RCTs), meta-analyses, systematic reviews, and national or international guidelines on infertility evaluation and treatment[3,4]. We prioritized publications that addressed practical, first-line strategies for common infertility etiologies and age-stratified management algorithms. References were organized by topic (definition and epidemiology, diagnostic evaluation, male- and female-specific causes, and treatment strategies) [5,9].

The synthesis was structured to reflect a **stepwise clinical pathway**, first outlining initial evaluation of both partners, then classifying major etiologic categories, and finally mapping corresponding management options. Tables were designed to summarize key diagnostic tests and treatment strategies by category for quick clinical reference.visualize[3,6].

1. RESULTS

1.1. Definition and timing of evaluation

Infertility is defined as failure to achieve pregnancy after 12 months of regular, unprotected intercourse. Earlier evaluation is recommended in women older than 35 years who have failed to conceive after 6 months and in women older than 40 years without delay, reflecting the age-related decline in fecundity[3,1]. Immediate evaluation is also warranted in women with oligomenorrhea, amenorrhea, prior pelvic inflammatory disease, endometriosis, tubal surgery, or suspected male factor infertility[3,8].

Population	Timing of evaluation
Women <35 years	12 months of unprotected intercourse [3,1]
Women 35–39 years	6 months of unprotected intercourse [3,1]
Women ≥40 years	Immediate evaluation [3,1]

Known risk factors (tubal disease, endometriosis, male factor) Earlier evaluation as clinically indicated[3,8]

1.2. Initial evaluation (both partners)

A structured infertility work-up begins with a detailed reproductive, sexual, menstrual, surgical, and medical history, followed by physical examination of both partners. Essential initial tests include:

- **Woman:** menstrual history, mid-luteal serum progesterone when ovulatory dysfunction is suspected, thyroid-stimulating hormone, and prolactin; hysterosalpingography (HSG) or sonohysterography (SHG) to assess tubal patency and uterine cavity when indicated[3,5].

- **Man:** semen analysis (repeat once if abnormal); total testosterone, FSH, and prolactin when severe oligo/azoospermia is found; genetic testing (karyotype, Y-microdeletions) when indicated[3,9].
- Ovarian reserve assessment (anti-müllerian hormone, day-3 FSH/estradiol, antral follicle count) is useful in women of advanced reproductive age or those with suspected diminished reserve[3,6].

1.3. Major etiologic categories and diagnostic findings

Approximately 85% of infertile couples have an identifiable cause, with common categories shown in the table below[3,6].

Category	Typical features	Diagnostic testing
Ovulatory dysfunction	Irregular/absent menses, PCOS	Menstrual history, mid-luteal progesterone, TSH, prolactin, androgen profile
Male factor	Abnormal semen parameters	Repeat semen analysis; FSH, testosterone, prolactin, genetic testing if severe/azoospermia
Tubal disease	History of PID, ectopic pregnancy, abdominal surgery	HSG, laparoscopy with chromopertubation if indicated
Uterine pathology	Submucosal fibroids, polyps, septum	TVUS, SHG, MRI/3D ultrasound
Endometriosis	Pelvic pain, dysmenorrhea, dyspareunia, adhesions	Clinical suspicion, transvaginal ultrasound, laparoscopy in selected cases
Diminished ovarian	Advanced age, prior	

reserve

Unexplained infertility chemotherapy, poor response to stimulation

Normal evaluation on standard work-up

AMH, day-3 FSH/estradiol, AFC

Diagnosis of exclusion after complete evaluation

Age and duration of infertility further refine prognosis and treatment intensity[3].

1.4. Management strategies by category

Ovulatory dysfunction (especially PCOS)

For anovulatory women, particularly those with PCOS, ovulation induction with **letrozole** is now preferred as first-line therapy; clomiphene citrate remains an alternative. Gonadotropins are reserved for women who fail oral agents or in whom close monitoring is available[3,6].

Male factor infertility

Mild-moderate male factor infertility may be managed with ovarian stimulation plus IUI, whereas severe oligospermia or azoospermia typically requires IVF-ICSI, often with surgical sperm retrieval in obstructive or non-obstructive azoospermia[3,9].

Tubal and uterine disease

Bilateral tubal obstruction or hydrosalpinx may be approached by tubal surgery or IVF; IVF is generally preferred in older women or those with other risk factors. Uterine pathology such as submucosal fibroids, polyps, or septum should be corrected hysteroscopically before starting ART[5,7].

Endometriosis

Laparoscopic surgery improves fertility in selected women with minimal–mild disease, while advanced disease often requires ovarian stimulation or IVF rather than expectant management[5,9].

Unexplained infertility

Couples with unexplained infertility are commonly offered 3–4 cycles of ovarian stimulation with IUI; if unsuccessful, IVF is indicated[1,6].

Diminished ovarian reserve and advanced age

In women older than 38–40 years or those with markedly reduced ovarian reserve, early IVF

is recommended to maximize the chance of success within a limited reproductive window. Counseling on prognosis and options such as donor gametes should be individualized and patient-centred[4,9].

2. DISCUSSION

This review synthesizes current evidence into a practical, stepwise algorithm for the diagnosis and management of infertility. The core principles align with WHO and ASRM-type recommendations: evaluation should be parallel (both partners), systematic, and tailored to clinical findings; treatment should be individualized according to age, prognosis, and resource availability [5,4,9].

A key finding is that **early identification of treatable causes**—such as ovulatory dysfunction, mild–moderate male factor, and correctable uterine lesions—can significantly improve cumulative pregnancy rates before proceeding to IVF-ICSI. Ovulation induction with letrozole in women with PCOS and IUI for couples with mild male factor or unexplained infertility are cost-effective first-line options in many settings[3,6].

Conversely, in women of advanced reproductive age, those with bilateral tubal disease, or those with severe male factor infertility, early IVF-ICSI is more cost-effective and reduces the emotional burden of repeated failed cycles. Age-related decline in ovarian reserve and implantation potential underpins the rationale for escalating to IVF earlier in older women[1,6].

The algorithm presented here can be converted into a **flowchart figure** suitable for inclusion in clinical-guideline or practice-oriented journals. It emphasizes least-invasive, evidence-based treatments first, with clear indications for early ART when appropriate[3,4].

Limitations of this review include the narrative, non-systematic design and the fact that availability and cost of IVF-ICSI vary widely across settings[4,9]. Most of the underlying evidence comes from high-income countries, and the performance of age-stratified algorithms in low-resource environments remains incompletely validated[4,7]. Future research should focus on context-specific adaptations and cost-effectiveness analyses of stepwise infertility management in such settings[4,9].

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