

Chapter 41

Infertility



What is the definition of infertility?

- Failure to conceive despite regular sexual intercourse without contraception at least for 1 year

What is the incidence of infertility in reproductive age group?

- 10–15% of the reproductive age group

What is the difference between primary and secondary infertility?

- Primary infertility: Couples who have not become pregnant after at least 1 year having regular sexual intercourse without using birth control methods
- Secondary infertility: A history of at least one pregnancy

What is the meaning of Fecundability?

- Fecundability is the probability of achieving a pregnancy within one menstrual cycle.

What is the meaning of Fecundity?

- Fecundity is the probability that a couple will conceive leading to a live birth in any given menstrual cycle.

What are the reasons for the increase in the demand for infertility services in recent years?

- Postponing marriage and child expectation at an advanced age.
- Artificial reproductive techniques (ART) are improved.
- Public awareness.
- Increased rate of tubal dysfunction as a result of increased sexually transmitted diseases.

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What are the changes in oocyte count, fertility rates, and spontaneous abortion rates in females from fetal life to advanced ages?

- The total germ cell number peaks at 20 weeks. Approximately 6–7 million oogonia in female fetus at 20th gestational week. Primordial follicle formation, a single layer of pregranulosa cells surrounds each oocyte and continues until just after birth.
- 300,000–400,000 oocytes at birth.
- Approximately 200,000 follicles remaining in the ovary at the puberty.
- In reproductive life, 400–500 oocytes are ovulated and others are destined to atresia.
- Follicle loss increases with advanced age.
- Fecundity decreases.
- ART success decreases with age.
- The live birth rate per embryo transfer is 41% for <35 age, 35% for 35–37 age, 25% for 38–40 age, 14% for 41–42 age, 6% for 43 age, 3% for >44 age.
- Spontaneous abortion rate in natural cycles is 7–15% under 30 years of age. 8–21% for 30–34 age; 17–28% for 35–39 and 32–52% for >40 age.
- Results are similar in ART cycles; the abortion rate for <35 age is <20%, 30% for 40 years, and >60% for > 44 age.

What is the percentage of male/female ratio among infertile couples?

- 30–40% male
- 40–50% women
- 10–15% non-identified

What are the causes of infertility?

- In couples
 - Male factor 35%
 - Tubal/pelvic 35%
 - Ovulatory dysfunction 15%
 - Idiopathic 10%
 - Other 5%
- In women
 - Tubal/pelvic 40%
 - Ovulatory dysfunction 40%
 - Idiopathic 10%
 - Other 10%

Which couples should consult the clinic for ovarian reserve?

- After 35 years old all infertile women
- People with unexplained infertility
- Having a family history of premature ovarian failure (POF)
- Smokers
- Poor response to exogenous gonadotropin treatment
- Ovulatory dysfunction
- Endometriosis

- Multiple fibroids
- History of previous pelvic inflammatory disease (PID), pelvic surgery, ectopic pregnancy

What is the basic anamnesis of the patient with female factor evaluation of infertility?

- Gravida, parity, previous pregnancy history (secondary infertility)
- Menstrual order/disorder, presence and severity of dysmenorrhea (such as endometriosis)
- Frequency of sexual intercourse, history of sexual dysfunction
- The duration of infertility, previous treatments and outcomes
- Previous history of surgery, PID, and sexually transmitted diseases
- Profession
- Smoking, alcohol, and drug use
- Thyroid diseases and systemic symptoms, galactorrhea, hirsutism
- Having a family history of premature ovarian failure (POF)

What should be considered in female factor evaluation and physical examination?

- Secondary sex characters
- Signs of androgen excess
- Presence of galactorrhea
- Thyroid enlargement, nodule
- Pelvic tenderness, mass, uterine size evaluation (bimanual examination, ultrasound)
- Cervical or vaginal anomaly, vaginal discharge, chlamydia
- Nodularity in Douglas

What are the ovarian reserve tests (ORT)?

- Basal follicle stimulating hormone (FSH) levels measured on day 3 of the menstrual cycle is the most widely used ORT to assess the ovarian response to stimulation (threshold is 25 IU/L).
- Anti-Mullerian hormone (AMH) is a hormone that is produced by granulosa cells of preantral (primary and secondary) and small antral follicles. AMH levels correlate with basal antral follicle count (AFC) (threshold is 0.2–1.26 ng/mL). It is important to note that AMH cannot be used as a marker to predict pregnancy.
- Women with a low day 3 inhibin B concentration (<45 pg/mL) have a poor response to superovulation for IVF and are less likely to conceive a clinical pregnancy.
- Basal estradiol (E2) > 70pg/mL indicates poor prognosis, an elevated basal E2 level may mask abnormal FSH levels.
- Clomiphene citrate challenge test (CCCT) is a dynamic test. On the 3rd day of the menstrual cycle, clomiphene citrate (CC) oral 2 × 50 mg/day (5–9) is given. Poor prognosis on day 3 FSH or day 10 FSH > 10 IU/L.
- Exogenous FSH ovarian reserve test is a dynamic test. On the 3rd day of the menstrual cycle, basal FSH and estradiol levels are measured and 300 IU FSH administered. The serum estradiol concentration is checked 24 h later.

- Number of antral follicles is checked by transvaginal ultrasonography in the early follicular phase. A count of 8–10 is considered as a predictor of a normal response.
- The ovarian volume which is measured by transvaginal ultrasonography remains unchanged till the perimenopausal period and does not add to the predictive value of antral follicle counting. Also ovarian Doppler flow during ovarian stimulation does not add to the predictive value of antral follicle counting.
- GnRH-agonist stimulation test involves the assessment of serum estradiol on day 2 of the cycle followed by the subcutaneous administration of GnRHa 100 µg. A change in estradiol levels is noted by repeating the test 24 h later on the 3rd day of the menstrual cycle. A rise in estradiol is considered to be indicative of good ovarian reserve.

What are the useful methods for determining ovulation?

- The absolute proof of ovulation is the formation of pregnancy.
- Disappearance or sudden decrease in follicle size detected by transvaginal ultrasonography. Detection of LH in urine.
- Basal body temperature (BBT) rises throughout the luteal phase, due to thermogenic effect of progesterone. In late luteal phase, when the corpus luteum regresses and serum progesterone level decreases, the BBT returns to the lower range within 1–2 days before, or just at, the onset of menstrual bleeding. The biphasic pattern of BBT retrospectively suggests ovulation.
- Mid-luteal progesterone measurement >3 ng/mL to detect ovulation.

Which blood tests are checked in patients with suspected ovulatory dysfunction?

- Amenorrhea: PRL, TSH, progestin challenge
- Perimenopause: FSH, E2
- Galactorrhea: TSH and PRL
- PCOS, acne, hirsutism, alopecia, male type hair loss: testosterone, dehydroepiandrosterone sulfate (DHEAS)
- Congenital Adrenal Hyperplasia (CAH): 17-OH progesterone
- Signs of hypothyroidism such as slowing of the metabolism, weight gaining, fatigue: TSH

Why and how to perform uterine factor examination in infertility examination?

- To examine the uterine cavity
- First transvaginal ultrasound is applied. In case of submucosal fibroids or endometrial polyps are suspected, then uterine cavity should be evaluated by saline infusion sonography (SIS).
- After SIS, if submucosal fibroids and polyps are observed then uterine cavity is reevaluated by hysteroscopy to see and treat. It is a definitive method.
- Also by hysterosalpingography (HSG) uterine cavity could be evaluated, and tubal patency could be checked as well.

What is the role of the uterine septum in infertility?

- Uterine anomalies 4.3% in general population, 3.5% in infertile patients, 13% recurrent pregnancy loss.
- Uterine septum is the worst obstetric outcome associated with recurrent pregnancy loss and obstetric complications.
- Most common congenital uterine anomalies (35%).
- The most common cause of obstetric complications.
- The relationship between primary infertility and septum has not been fully elucidated, but high pregnancy rates have been reported in infertile patients after hysteroscopic metroplasty.

What is the role of the fibroids in infertility?

- Whether fibroids reduce fertility is controversial.
- Possible mechanisms: Cornual occlusion. Dysfunctional uterine contraction prevents sperm or ovum transport. Embryo implantation is reduced as a result of reduced regional blood supply.
- Submucous fibroids: hysteroscopic myomectomy
- Intramural fibroids: controversial
- Subserous fibroids: follow-up

What is the role of endometrial polyps in infertility?

- The effect on fertility is not known.
- Hysteroscopic polypectomy, in case of >1 cm and in symptomatic polyps

What is the role of tubal factor in infertility?

- The most common cause of infertility in infertile couples (35%).
- History of PID, septic abortion, ruptured appendicitis, tubal surgery, ectopic pregnancy, tubal damage.
- PID is the major cause of tubal factor infertility.

What is the role of PID on tubal infertility?

- The incidence of tubal infertility after a PID episode is 10–12%, 23–35% after the second, and 54–75% after the third.
- Most patients with tubal disease do not have a history of pelvic infection, but quiescent ascending infection is the most common cause.

Which imaging methods are used to investigate tubal factor in infertility?

- HSG
- Laparoscopy and hysteroscopy
- Transvaginal hydrolaparoscopy

What is the role of HSG in the evaluation of tubal factor in infertility?

- 65% sensitivity and 83% specificity for testing tubal patency.
- 38% chance of tubal obstruction if HSG is abnormal.
- If HSG is normal, the probability of tubal openness is 94%.
- Normal HSG is more reliable.

What is the role of laparoscopy (L/S) in the evaluation of tubal factor in infertility?

- Gold standard to show tubal patency. See and treat.
- HSG shows the uterine cavity and the tubal patency, as for L/S shows intra-abdominal adhesions, endometriosis, and ovarian pathologies, as well.

What is the role of the male factor in infertility?

- It constitutes 35% of the causes of infertility.

What is the basic anamnesis of the patient with male factor evaluation of infertility?

- Anamnesis of previous fertility, presence of chronic disease, previous urogenital infection and surgery, alcohol, drug use, libido, coitus frequency, toxic substance or radiation exposure.

What is the basic physical examination of the patient with male factor evaluation of infertility?

- Physical examination: Varicocele, urethral meatus, vas deferens, secondary sex characters

What are the components of male infertility etiology?

- The cause is unidentified → 31%
- Varicocele → 15.6%
- Hypogonadism → 9%
- Subclinical infertility → 8%
- Undescended testis → 7.8%
- Erectile dysfunction → 6%
- Immunological → 4.5%
- Systemic diseases → 3.1%
- Obstructive pathologies → 1.7%
- Other causes → 13%

What are the recommendations prior to semen analysis?

- After 2–3 days of abstinence.
- Ejaculate material is put into a clean container.
- Inspection within 1 h of collection.
- Abnormal test results should be repeated after 3 weeks.

What is the meaning of aspermia?

- Complete lack of semen with ejaculation

What is the meaning of azoospermia?

- No sperm in the semen

What is the meaning of oligospermia?

- <15 million/mL of sperm count in ejaculate

What is the meaning of severe oligospermia?

- <5 million/mL of sperm count in ejaculate

What is the meaning of asthenospermia?

- Low sperm motility: If there is no motile sperm, a sperm viability test should be performed.

What is the meaning of teratospermia?

- Sperm morphology in the ejaculate is called abnormal.

What are the treatment recommendations for unexplained infertility in <35-year-old patients and older 35-year-old patients?

- <35 years: follow-up without treatment for 6–12 months up to 24 months as well in 20–25-year-old patients
- >35 years: gonadotropin + IVF

What are the criteria to apply IVF?

- Oligoasthenospermia-azoospermia not responding to hormonal treatment.
- Bilateral complete tubal obstruction, primary ciliary dyskinesia.
- Severe pelvic adhesion is detected and cannot conceive 1 year after tubal surgery.
- Advanced stage endometriosis.
- Unexplained infertility.

Suggested Reading

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