Is defined as the inability of the couples to conceive after one to two years of unprotected intercourse .

Incidence : ≈ 10 – 15 % of couples have infertility

Types of infertility :

a. **Primary** (70 %) no previous history of pregnancy .

b. **Secondary** (30%) with previous history of pregnancy regardless the fate of this pregnancy e.g miscarriage , ectopic , term .

* **Causes of infertility** : in general divided in to five major categories :

1. Anovulation
2. Male
3. Tubal
4. Endometriosis
5. Unexplained .

So ≈ 65% of infertility female factors , 35% is male factors (50%due to identified causes) and 50% unexplained types .

1.Anovulation : classification of anovulation

- WHO type I : hypogonadotrophic , hypo - oestrogenic central cause with low FSH , LH , oestradiol but normal prolactin .

- WHO type II : normogonadotrophic normo-oestrogenic and normal prolactin mainly due to PCOS .

- WHO type III : hypergonadotrophic hypo-oestrogenic due to ovarian failure , high FSH , LH , low oestradiol but normal prolactin .

- WHO type IV: hyperprolactinemia central cause high prolactin with low FSH , LH and oestradiol .

2. Tubal causes : mainly presented as secondary type of infertility , this either tubal blockage or tubal dysfunction due to – infection and pelvic inflammatory disease e.g chlamydial infection .

- **Pelvic surgery**
- **Corneal fibroid or polyps**
- **Endometriosis**
- **Infection due to IUCD**

3. Unexplained : 50% of couples presented with no identified single cause after full investigations .

* **Poor prognostic factor of infertility** :

1. primary type
2. long duration ≥ 3 years
3. female age > 30 years
4. tubal causes
5. male factor
6. endometriosis

* **Management of couples with infertility** :

A) **History** : for female : age , type of infertility any previous investigations , previous treatment , previous contraception .

- menstrual history , length of cycle amenorrhoea , oligomenorrhoea , dysmenorrhoea , menorrhagoea . intermenstrual bleeding .
- obstetrical history previous pregnancy miscarriage , ectopic , termination of pregnancy .
- medical history : chronic illness , drug use , previous PID , galactorrhoea , DM , HPT .
- Surgical history : tubal surgery , ovarian surgery other pelvic surgery .

B) **examination** : general examination for height , weight , body mass index , blood pressure , fat and hair distribution , acne , galactorrhoea .

- local examination : for scars , abdominal masses .
- pelvic examination : inspection of external genitalia speculum examination , vaginal assessment for infections , septa , cervix for infection , polyps , and bimanual examination of uterus size , shape , position mobility , presence of adnexal mass and tenderness .

C) **Investigation** :

1. investigations for anovulation :

- hormonal study , in case of regular cycle and length every 28 days , we measure the progesterone level at day 21 of cycle (mid.luteal level) it should be ≥ 30nmol/L , while in case of regular cycle but longer than 28 days – 35 days so we measure the level at day 21 then weekly continued until next period .

In case of irregular cycle , oligomenorrhoea and amenorrhoea , there is no benefit to measure the progesterone level but measure the level of FSH , LH , TSH , prolactin , Testosterone , DHEAS , oestradiol and sex hormone binding globulin .

U/S : to detect the signs of ovulation in combination with hormonal study , diagnosis of PCOS , ovarian cyst , endometrioid cyst , fibroid , polyp and adhesions .

2. investigations for tubal factors : assessment of tubal patency in women is ovulating and semen parameters are satisfactory is indicated by either Hysterosalpingography HSG by using radiopaque iodine-based dye through the cervix and pelvic X-ray **or** laparoscopic and dye (investigation of the choice) by direct visualization of spillage of the dye and also assessment of pelvic cavity for adhesions , endometriosis …. ect.

3. Hysteroscopy : to assess uterine pathology such as adhesion , polyps , submucous fibroid this can used for therapeutic rule also like myomectomy , polypectomy and adhesiolysis.

4. post-coital test : to detect the presence of motile sperm now it less used because it not specific test .

5. endometrial biopsy : at luteal phase to assess ovulation also it not established in routine practice .

6. screening for chlamydia and other PID .

7. ovarian reserve : by measuring based FSH level at day 3 of cycle and inhibin level in combination with U/S for ovarian size , to assess the patient response for ovulation stimulation treatment .

* **Treatment of Infertility** : all couples trying for pregnancy will benefit from some general advice such as cessation of smoking and limiting alcohol intake , advice about general lifestyle measures including the need to achieve optimum BMI .

Preconceptaul dietary supplementation of folate to reduce the risk of neural tube defect .

A. **treatment of anovulation** :

- **WHO type I** : the most physiological treatment of this type is with pulsatile administration of GnRH agonists either s.c or iv then monitoring is performed by hormonal assay and pelvic U/S to check size of follicles at day 13 of cycle (it should be at least ≥ 16mm size of follicles) , then luteal phase support by HCG injections pregnancy rate of 80-90% over 12 cycles of treatment .

- **WHO type II** (PCOS) :

1. Weight loss and dietary measures : this is first line of treatment in obese women with anovulation due to PCOS central obesity and high BMI are important predisposing factors for insulin resistance Hyperinsulinemia and hyperandrogenaemia , so loss of 5-10% of body weight may be enough to restore reproductive function in 50-100 % women within 6 months .

2. Metformin (either alone or with clomifene citrate) , the strong association between anovulation and insulin resistance/hyperinsulinaemia led to lowering insulin level would lead to improvement in the clinical and metabolic profile in women with PCOS , metformin is an oral biguanide which has been used for the treatment of hyperglycemia in maturity onset diabetic but which does not lower glucose level in euglycemic subjects . its action include decrease insulin level and increase the sensitivity to insulin , the starting dose 500 mg once daily increasing gradually to 500mg trice daily or 850mg twice daily . for at least 3-6 months , long term effect of metformin in PCOS it reduce blood pressure and reduce low-density lipoprotein .

3. Clomifene citrate : orally active synthetic non-steroidal compound with oestrogenic as well as anti-oestrogenic properties . it displaces oestrogen from its receptors in the hypothalamic-pituitary axis , reduce the -ve feedback effect of oestrogen and encourages GnRH secretion , it is administration in an initial dose of 50mg on days 2-6 of cycles (either spontaneous or induced menstrual cycle) the dose can be increase by 50mg up to maximum of 150 mg pre day , couples are advised to have intercourse every other day from day from day 9 of the cycle for at least one week course of treatment 6-12 cycles can be used in women who respond to the drug , monitoring by U/S for follicular development and ovulation , pregnancy rate ≈ 40% .

- Side effects : thickening of cervical mucus (if dose ≥ 100mg /day) hot flushes , nausea , vomiting , headache , blurred vision . multiple pregnancy ≈ 7-10% OHSS < 1 % .
- Other similar drug is tamoxifen .

Gonadotrophines : is used to women do not respond to clomifene citrate or fail to conceive after 6-12 ovulatory cycles used either combined FSH , LH or highly purified FSH starting dose 75 Iu alternative days and increase gradually . route either s.c or im . it has 30% risk of multiple pregnancy and ≈ 4.6% risk of OHSS . course of RX in 6-12 cycles , pregnancy rate ≈ 50 % .

5. Aromatase inhibitors : it used as alternative to clomifene in view of lack of anti-oestrogenic effects eg anastrazole and letrazole .

6. Laparoscopic ovarian drilling it effective like GnRH (50 %) with no complication of multiple pregnancy or OHSS .

- Who type III : treatment by Egg donation.
- Who type IV : treated as hyper-prolactiaemia .

B) Tubal causes :

1. mild : tubal surgery , proximal tubal obstruction treated by tubal cannulation.
2. Moderate to severe : in vitro fertilization (IVF)

B. Unexplained infertility : empirical treatment by low dose clomifene citrate with intra-uterine insemination (IUI) .

NOTES :

- The comments cause of female infertility is tubal factor .
- The comments cause of tubal disease is PID
- The comments cause of PID is chlamydial infection
- The comments cause of anovulation infertility is PCOS .

Thank you