An overview of infertility
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Infertility is a condition that causes considerable psychological distress to the couples. Even though the exact prevalence of infertility in Bangladesh is difficult to ascertain, it affects 10 to 15% couples in the western world.\(^1\) There has not been any major increase in the prevalence of infertility in recent years, but there is a greater awareness of the problem and also availability of more effective treatments like in vitro fertilization even in countries like Bangladesh.

Epidemiological data indicate that conception occurs in 84% of women within 12 months and 92% by second year of ceasing contraception.\(^1\) So infertility can be defined as inability to conceive after one or two years of regular unprotected sexual intercourse. It can be broadly divided into primary infertility where couples have never conceived previously and secondary infertility where couples have had a pregnancy, although not necessary a successful one.

Either the male and female partners can be responsible for infertility in around 30% cases or both are involved in another 25 to 30% cases. In the remaining 10 to 15% case, no cause could be found out, which is known as unexplained infertility.

Semen analysis remains the most important aspect of male investigations. World Health Organization values for definition of normality are widely accepted.\(^3\) Additional investigations are required if semen report fail to meet these criteria. Serum FSH differentiates between obstructive and non-obstructive azoospermia and has enormous prognostic value if ICSI (intracytoplasmic sperm injection) is to be considered. Serum testosterone is only indicated in suspected hypogonadism. Serum prolactin is suggested in men with coital difficulty. Semen culture is only required if there is microscopic evidence of infection.

Investigations to find out the capacity of sperm to fertilize an ovum are difficult to interpret. Even though post coital test is useful providing information about sperm function, systemic review of literature suggests that this test lacks validity for routine use.

Significance of antisperm antibody present in serum or semen is unclear. It mostly develops following vasectomy or infections like epididymitis or orchitis. It is of clinical importance if reversal is required.

Imaging of the male genital tract include thermography, Doppler USG or retrograde venography to diagnose varicocele. In obstructive azoospermia, vasography may be suggested in order to find out the site of obstruction. Testicular biopsy has been virtually replaced by serum FSH estimation.

About 15% azoospermic men are found to have abnormal karyotype like Klinefelter's syndrome. So karyotyping may be suggested in men with azoospermia or severe oligospermia.

During management of male infertility, men should be advised to reduce alcohol intake, stop smoking and use or recreational drugs which interfere with fertility.

There are various treatments for male infertility. Even though the WHO suggests that there is an inverse relationship between semen quality and the presence and severity of varicocele, at present there is no evidence that surgical treatment of clinically detectable varicocele with oligospermia improves

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pregnancy outcome. Hypogonadotropic hypogonadism in men can be successfully treated with exogenous gonadotrophin or GnRH therapy. Ejaculatory problems are often treated with alpha adrenergic and anticholinergic drugs.

Acute bacterial infection of the genital tract should be treated with antibiotic even though there is no evidence that antibiotics improve male fertility. Epididymovasostomy is suggested in post vasectomy cases. Orchidopexy is suggested when ever there is testicular maldescent.

There are various empirical treatments for male infertility which has not shown to be effective. There is no evidence to recommend gonadotropin, GnRh, testosterone, anti estrogens like clomiphen or tamoxifan in treatment of male infertility. Bromocriptine is only beneficial in men with hyper prolactenemia. Antioxidants like glutathione, vitamin E and C may improve semen parameters but this mode of treatment requires further evaluation. Systemic steroid therapy does not improve immunological male infertility and it is not recommended.

Assisted reproduction has great role in male infertility. IUI (intrauterine insemination) improves the relative odds of pregnancy if semen parameters are abnormal, even though the pregnancy rates remain low (4-6%) 6. Men with severe sperm abnormalities or non-obstructive azoospermia now can be managed by microsurgical sperm retrieval with ICSI (Intra Cytoplasm Sperm Injection) but it puts the female under hazard of assisted reproduction.

Regarding females, investigations are done to find out if the woman is ovulating. Laboratory evidence may be obtained through measurement of serum progesterone in the luteal phase of menstrual cycle. If there is history of irregular menstruation or periods of amenorrhoea, especially associated with obesity, hirsutism or galactorrhoea, additional biochemical tests like serum FSH, LH, TSH and prolactin in early follicular phase should be done.

When the preliminary investigations suggest that the woman is ovulating and sperm production is satisfactory, pelvic assessment should be undertaken. If there is identifiable risk factors for pelvic pathology like past history of pelvic inflammatory disease, previous ectopic pregnancy or symptoms suggestive of endometriosis, either hysterosalpingography or laparoscopy with dye hydrotubation is advised. Sonohysterography, an alternate outpatient investigation may be used as well but it has yet to gain widespread popularity.

Treatment of ovulatory failure depends upon the cause. In WHO group I ovulatory dysfunction (due to hypothalamo pituitary failure), weight gain is the most effective treatment if there is significant weight loss. Use of pulsatile GnRh agonist is mainly indicated where endogenous GnRh levels are very low. In hyperprolactenemia, medical therapy including bromocriptine, cabergoline or quinigalide are most effective to reduce the prolactin level. Surgery is required when there is large macro adenoma.

In type II ovulatory failure (mainly PCOS) treatment options include, weight loss and lifestyle modification. Insulin sensitizing agents like metformin reverse some of the metabolic effects of PCOS (Polycystic ovary syndrome) and act as pre-treatment and co-treatment agent with anti estrogens. Clomifene is most widely used anti estrogen. Multiple pregnancy can occur in around 7 to 10% cases and mainly involves twins. OHSS (Ovarian hyper stimulation syndrome) is rare. A distant link with ovarian cancer has been described in women receiving more than 12 cycles of clomifene, so it should be used to the lowest effective dose and duration of use. Gonadotropins (hMG, purified FSH, recombinant FSH) are used when patient fail to ovulate with clomiphen with or without metformin. Miscarriage rate is quite high (25-30%) in gonadotropin ovulation induction. Multiple pregnancy rate is 15 to 20% and rate
of OHSS is 1-2%.8. Recently aromatase inhibitors like letrozol are used in anovulatory women with PCOS who are resistant to clomifene but large randomized trials are required to investigate its effectiveness. Laparoscopic ovarian drilling is widely used now days. It results in mono follicular ovulation which means the risk of OHSS and multiple pregnancies can be avoided. It also increases ovarian sensitivity to subsequent treatment with clomifene. There has been no evidence of premature menopause for women followed up for over 10 years.6

Egg donation is the only treatment option for type III ovulatory failure (Ovarian failure).

In case of infertility due to tubal cause, medical treatment has limited values. Chemotherapy has a definite role in cases of tuberculosis even though it will not reverse the damage present. Surgery offers the best results when carried out in properly selected cases. Salphingography with tubal catheterization or histeroscopic tubal recanalization can be the treatment options. Compared to IVF (In vitro fertilization), tubal surgery carries no risk of OHSS and a lower risk of multiple pregnancies and miscarriage, even though ectopic pregnancy is a possible outcome with all surgical techniques. Most cases of tubal sterilization can be treated with tubal reanastomosis. IVF is the first-line treatment if there is moderate to severe tubal disease and should be discussed if pregnancy does not occur 12 to 18 months after surgery.

Endometriosis is commonly associated with infertility. Medical treatment has no role in endometriosis related infertility9. Surgery is often the only treatment but in cases of moderate and severe disease, assisted reproductive techniques should be considered as an alternative or after unsuccessful surgical treatment.

Effective treatment of unexplained infertility includes super ovulation and intrauterine insemination and in vitro fertilization. A Meta analysis has demonstrated statistically significant benefit following treatment with clomifene in unexplained infertility.10

Significant developments have taken place in the field of assisted reproduction over the last 15 years. IUI (intra uterine insemination) involves timed introduction of washed motile sperm into the uterine cavity. It is a relatively less invasive procedure which is considered in cases of mild male infertility, unexplained infertility and coital or ejaculatory failure. IVF is a method of assisted reproduction when the sperm and oocytes are mixed to allow fertilization to occur in vitro. The resulting embryos are then transferred into the uterus. Success rate of IVF has risen significantly during the course or last 10 years and have reached 28.8% live birth rate/embryo transfer for women under the age of 38 years and 24.3% for all age groups.11 Lastly the advent of ICSI (intracytoplasmic sperm injection) has revolutionized the management of couples suffering from severe male factor infertility.

There has been a vast improvement in the management of infertility in the last 20 years. The rational use of different drugs, surgery and newer IVF techniques holds the promise of a solution for many infertile couples. But for clinicians, it is also a challenge to deploy these new techniques safely and effectively. So adequate evaluation must be done before they are used in routine clinical practice.

References
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