

Ayurlog: National Journal of Research in Ayurved Science*A Web based quarterly online published Open Access peer reviewed National E-journal of Ayurved***A review of Female Infertility:
important etiological factors and its treatment**

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Abstract:

Infertility is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. Infertility is a worldwide concern which affects the peoples of all communities. The cause and magnitude of infertility may vary with geographical location and socio-economic status. It is estimated that approximately 8-10% of couples within the reproductive age group present for medical assessment, generally following two years of failed efforts to reproduce. In India alone, 15-20 million couples suffer from infertility. Majority of cases the infertility is avoidable. In the past medical treatment for infertility particularly in cases of azoospermia, tubal blockage and other cases where the causes could not be

defined, had not been very successful. But with advancement of knowledge of reproductive physiology and availability of sensitive and specific diagnostic methods, this situation is changing very fast. A number of clinics specializing in infertility management have come up which offer a wider range of treatment options. The treatment options for infertility are increasing day by day. Keeping above scenario in mind, there is a need to review the various works done by researchers and various treatment modalities available. In this review the contributions of the different etiological factors in female infertility was looked into and attempt was made to update the available information on the management of female infertility. The main aim of this review is to generate

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information which could act as guideline in the evaluation of female infertility.

Introduction:

"Infertility will become more common in future generations with more couples needing help to have a baby,"-*BMJ*

Infertility can be defined clinically as a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse¹. Infertility affects both men and women of reproductive age group all over the world leading to personal suffering and disruption of family life. Interventions and care for people with infertility have been mostly sidelined to the area of private medicine, with 'infertility' often described as a 'rich person's disease'.

The infertility can be primary or secondary. If the couple has never conceived despite cohabitation and exposure to pregnancy (not contracepting) for a period of two years, it is called primary infertility; primary infertility is also referred to as primary sterility. If a

couple fails to conceive following a previous pregnancy, despite cohabitation and exposure to pregnancy (in the absence of contraception, breastfeeding or postpartum amenorrhea) for a period of two years, it is secondary infertility; this is also known as secondary sterility.²

In the past medical treatment for infertility particularly in cases of azoospermia, tubal blockage and other cases where the causes could not be defined, had not been very successful. But with advancement of knowledge of reproductive physiology and availability of sensitive and specific diagnostic methods, this situation is changing very fast. In this review the contributions of the different etiological factors in female infertility was looked into and attempt was made to update the available information on the management of female infertility.

Magnitude of the problem of infertility:

Infertility is a world-wide problem affecting people of all communities. The causes and magnitude of it may with geographical location and socio-economic status. Approximately 8-10% of couples within the reproductive age group present

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for medical assessment, generally following two years of failed efforts to reproduce³. As per WHO, using new infertility prevalence calculation, it is estimated that one in every four couples in developing countries had been found to be affected by infertility, when an evaluation of responses from women in Demographic and Health Surveys from 1990 was completed in collaboration with WHO in 2004.⁵ In India prevalence of primary infertility was estimated to be approximately 3% whereas secondary infertility is 8%.⁶ More recently a study carried out by Adamson et al estimated that prevalence of primary infertility is 12%.⁷

Causes of Infertility:

The infertility could be primary when the couple has not conceived even once or secondary when the couple has conceived at least once but is unable to conceive again for two years or more. The major causes of infertility include tubal disease, congenital abnormalities, ovulatory dysfunction, endometriosis, immunological factors, and sexual

dysfunction or many a times it could be unexplained.

The endocrine causes such as anovulatory oligomenorrhoea, amenorrhoea with normal or low endogenous gonadal and pituitary hormones, and anovulation and irregular cycles were the second most common cause (38%) of female infertility.

In about 35% of women, the cause of infertility was categorised as unexplained.

In males, no demonstrable cause is most common diagnosis seen in almost 50% of the infertile men. Some studies have even reported no specific cause in as many as 80% of infertile men¹⁰ and sperm dysfunction in 24 % cases¹¹. This is probably due to lack of knowledge of male reproductive physiology and pathology.

Male factor infertility reflects a variety of pathogenetic factors, predominantly defective sperm production, sperm dysfunction and impaired transport¹². Defective sperm morphology and deposition can be congenital, immunological, infective, neurogenic or psychological factors.

Treatment options for infertility:

Treatment plans are based on the diagnosis, duration of infertility, and the

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woman's age. Management of any underlying female and/or male factors affecting fertility may include medical treatment (eg, pharmacotherapy), surgical intervention, ART.

Pharmacological Treatment:

Clomiphene citrate: It is a nonsteroidal estrogen capable of binding with estrogen receptor-binding proteins in a manner similar to estrogen.¹³ It behaves similar to an antiestrogen. Its mechanism of action is still not well understood, but it competes for the estrogen receptor at the hypothalamus, pituitary, and ovarian levels. Because of the action at the estrogen receptor level within the hypothalamus, CC alleviates the negative feedback effect exerted by endogenous estrogens. As a result, CC normalizes the GnRH release; and re establish the normal process of ovulation.¹⁴ The standard dose of CC is 50 mg PO qd for 5 days, starting on the menstrual cycle day 35 or after progestin induced bleeding. As an antiestrogen, CC requires that the patient have some circulating estrogen levels; Otherwise, the patient will not respond to the treatment.

Aromatase inhibitors: Aromatase inhibitors (letrozole, anastrozole) inhibit the action of the enzyme aromatase, which converts androgens into estrogens by a process called aromatization. Aromatase inhibitors are available for clinical use and FDA approved for treatment of postmenopausal breast cancer, but not for ovulation induction.

Human gonadotropins: The new generations of available gonadotropins are produced by genetically engineered mammalian cells (ie, Chinese hamster ovary cells), in which the gene coding for the alpha and beta FSH subunits has been inserted (follitropin alfa and follitropin beta).²⁰

Synthetic GnRH: Synthetic GnRH (gonadorelin) has a chemical composition similar to native GnRH and is indicated for patients with hypothalamic dysfunction, especially those who do not respond to CC.²¹ This drug is administered in a pulsatile fashion every 60-120 minutes, intravenously or subcutaneously using a delivery pump. The starting dose is 5 mcg per pulse intravenously or 5-25 mcg subcutaneously.

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GnRHa antagonists: The GnRHa antagonists are the latest generation of GnRHa that block LH secretion without a flareup effect.²² The GnRHa antagonists include cetorelix, ganirelix. GnRHa antagonists have the advantage of blocking the LH surge at the periovulatory period; therefore, premature luteinization or spontaneous LH surge does not occur. Because the pituitary gland is not downregulated at the beginning of the menstrual cycle, smaller amounts of gonadotropins are required to stimulate ovulation.

Assisted Reproductive Technologies (ART)

The first successful human IVF attempt resulted in the 1978 delivery of Louise Brown in England and is considered the beginning of a new era for the treatment of infertility.²³

Assisted reproductive technologies used to treat infertility include the following:

In vitro fertilization (IVF): IVF consists of retrieving a preovulatory oocyte from the ovary and fertilizing it with sperm in the laboratory, with subsequent embryo transfer (replacement) within the endometrial cavity. Biologists and

veterinarians have used IVF for several decades in the laboratory for applications such as animal husbandry and cattle breeding. Lack of understanding of human embryo development and special metabolic needs accounted for the delay in achieving success. The pioneering work of Edwards and Steptoe has been duplicated worldwide, and IVF is now recognized as an established treatment for infertility.

Indications

Absence of the fallopian tubes and severe pelvic adhesions were the absolute indications for IVF, but they have been broadened. Patients with a history of endometriosis unsuccessfully treated medically or surgically can undergo IVF. Patients with some malformation of the uterus related to DES exposure during pregnancy are candidates. Patients with husbands who have severe oligospermia or a history of obstructive azoospermia are also candidates for IVF. Finally, patients who have failed more conservative therapies or with an unknown etiology of infertility (ie, NICs) may undergo IVF.²⁴

Gamete intrafallopian transfer (GIFT):

The procedure consists of ovarian stimulation, monitored follicular

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development, and oocyte aspiration similar to IVF. It differs in that the patient must have at least 1 normal appearing and patent fallopian tube.

Zygote intrafallopian transfer (ZIFT):

The zygote intrafallopian transfer (ZIFT) procedure is a combination of IVF and GIFT.²⁵ Fertilization occurs in the IVF laboratory. However, the preembryo is transferred into the fallopian tube via laparoscopy at the 2 pronuclei stage or 24 hours after oocyte retrieval.

Intrauterine insemination (IUI):

Intrauterine insemination (IUI) is a fertility treatment that involves placing sperm inside a woman's uterus to facilitate fertilization. The goal of IUI is to increase the number of sperm that reach the fallopian tubes and subsequently increase the chance of fertilization.

Alternative treatment plans

If pregnancy has not been established within a reasonable time, consider further evaluation and/or an alternative treatment plan, such as use of donor oocyte, sperm, or embryo, or the use of a gestational carrier or surrogate mother.

Gestational carriers:

A gestational carrier is a woman who is carrying a pregnancy resulting from embryos created by IVF, using the gametes of the intended parents.

Adverse Outcomes of Infertility**Treatment:**

Although infertility treatment, including ART, is generally safe, adverse outcomes have been described both in women undergoing ART and in infants born from these procedures. In conclusion, the problem of infertility is not a private sorrow. It is global problem whose magnitude is bound to increase in near future..

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