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Introduction

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2. Initial Workup and Diagnosis
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- The infertile couple
- Many times unmanageable
- As treatment is sometimes unbearable
- It starts with examination of couple
- With ultrasonography of female
- Including blood tests, urine as a routine
- Do semen analysis of male partner
- If it is OK then proceed further
- Then test the tube with SSG, HSG
- If hormonal abnormality, March on hormonal therapy



- Go for endoscopy, i.e., laparoscopy and hysteroscopy
- To find out the cause of infertility
- If all efforts are in vain
- Some ray of hope still remain, i.e., assisted reproduction
- IVF-ET, ICSI, GIFT, MIST
- There are still donor embryos-eggs
- So you have involved your leg
- Deeper and deeper
- Try for frozen embryos or co-cultures
- Advice for a surrogate mother
- If again no conception
- Give a wise decision of adoption!

■ INTRODUCTION

Infertility is a global issue. Couples from all levels of society come to clinician. The only statement from them is *“Doctor, do anything but we want a child!”*

Human reproduction is a complex system. If we look at the system carefully, then we also give credits to Almighty God or nature that though it is complex, every system is hormoneously organized. All hormones are in tune and rhythm. Endocrinal, reproductive and body's defensive systems are all working synergistically.

Incidence of infertility is about 15% in the population and increasing. We call a couple infertile when there is no pregnancy after 1 year of marriage without using contraceptive with regular sexual practice. So, it is very important that the couple should be aware of it. In infertility, mind and psyche both are involved along with body. And, in many communities, it is a social taboo. The couple always keeps on telling you that “Doctor, do whatever but we want affirmative results, i.e., child.”

Infertile couple is always in stress and strain. Many of the couples are wandering from one doctor to another. Some of them are lucky enough to get a proper treatment. But infertility is such a problem that many faculties with little knowledge treat it. And when all efforts are in vain then the couple comes to an infertility specialist.

Most of the patients, when they come to us, have pile of files with them. It is very difficult to go through all files when clinician is busy in the outpatient department (OPD) where a large crowd is in the waiting room. But, one should make a habit to have a look at the files and try to go through it in a short span. Note down the important points in your own file. While going through the files, if for a moment you look at them, then you will notice that most of the couples have very high hopes on their faces, i.e., for a child. Some are desperate. Some will say that we have no hopes but someone has recommended your name, so as a last try, we have approached to you. And, your tension and responsibility goes on increasing.

In other branches of our obstetric and gynecology, we have very bright options in treating patients, e.g., antenatal care (ANC) patients, gynecological problems like prolapse uterus, abnormal uterine bleeding (AUB), and fibroid. But, treating infertility is many a times frustrating for the clinicians as well as patients. Because, they demand a new live creation either naturally or artificially, i.e., a child.

So, when an infertile couple comes to your center since beginning, i.e., from reception, they have to be treated nicely. It is a usual complaint of the patient that they have been sitting in the waiting hall since hours. In a busy infertility clinic, it is not possible for the clinician to do a perfect time management. But, at least use kind words, give them adequate time and always explain the plan of treatment.

Many newly married couples rush to infertility center for treatment within 3–6 months. Counsel them that only 15% conceive in 1st month, 50% in 6 months, 75% in 1 year and 90% at the end of 2 years.

Always insist the couple to come together and examine husband and wife by andrologist and gynecologist,

respectively. After that counsel them together and explain regarding the female reproductive system; particularly ovulation, and importance of tubal, uterine factors.

Divide the couple in various categories like newly married young couples, couple with secondary infertility, couple with age between 30–35 years and above 35 years, female having major problems like tubal blockage/endometriosis/diminished ovarian reserve and male with abnormal semen parameters. Broadly, we can divide but the couple can present in any combinations.

Day-by-day, the science and technology are advancing. But along with that, infertility is also on rising trend.

■ WHY RISING TREND IN INFERTILITY?

While couple is demanding child, we cannot forget certain important things before starting major investigations.

- Changing lifestyle
- Stress-induced infertility
- Environmental and occupational hazards and modern gadgets

Changing lifestyle and stress-induced infertility go hand-in-hand.

Changing Lifestyle

Modern lifestyle, advanced age of couple, smoking, alcohol, obesity, lack of exercise, poor diet and stress are important factors which affects fertility.

- Age of the couple to enter into the parenthood is increasing. As the age of female increases above 30, the number of oocytes starts declining. In men, semen parameters also begin to get a steady decline as early as 35 years and after

40 years, even more DNA damage is seen in their sperms. Marital conflicts and remarriages are increasing.

- Consumption of saturated fatty acids, trans fats instead of monounsaturated fats in the diet has been demonstrated to increase the risk of anovulatory infertility.
- Obesity and sedentary lifestyle cause increase in body mass index (BMI) leading to polycystic ovarian syndrome (PCOS). It will lead to anovulatory cycles, inadequate endometrial response and implantation failure.
- Moderate exercise is always necessary. But strenuous exercise more than 5–6 hours per week is associated with low sperm count in men and higher rate of cycle cancellation, implantation failure in IVF.
- Smoking, tobacco and alcohol also affect male as well as female fertility. Cigarette smoke affects sperm activity and leads to decreased fertilization capacity. In females, it causes decreased ovarian function and reduction in ovarian reserve.

Stress Gives Rise to Infertility and Vice Versa

- Prolonged stress will activate hypothalamopituitary adrenal axis and inhibits hypothalamic–pituitary–gonadal axis.
- In female, it will cause functional hypothalamic amenorrhea and functional hypothalamic anovulation. This persistent suppression will lead to ovarian quiescence, amenorrhea and infertility.
- In male, it will decrease testosterone levels affecting ejaculation and sperm parameters.
- Stress can be professional, emotional, psychological, environmental, medical disease, familial, financial, and infertility related. All are related to each other in some aspect.

Environmental and Occupational Hazards and Modern Gadgets

Day-by-day, environment and occupational hazards are affecting male and female infertility.

- Radiofrequency, electromagnetic waves (RFEMW) utilized by cell phones have detrimental effects on fertility.
- Soft plastic and plasticizers are also supposed to affect sperm motility.
- Bisphenol is used to produce plastic polymers and used in barrier coatings for the inner surfaces of food and beverage cans. It is endocrinal disruptor and causes male infertility. In females, it produces insulin resistance leading to polycystic ovarian syndrome.
- Lead used in batteries, paints, ceramics, pipes. Mercury used in thermometers, batteries. Boron in glass, cement, soaps. All these metals interrupt hypothalamic-pituitary axis causing subfertility.
- Pesticides and insecticides use has increased, thus affecting fertility.

The whole world is moving toward industrialization. Due to career, stress, luxurious lifestyles, there has been dramatic

IN NUTSHELL

- Infertility involves many specialties, involving body and mind.
- Initial couple counseling, examination, evaluation and management plan is very important.
- Stress-induced infertility and infertility counseling stress go hand-in-hand together.
- There is a rising trend of infertility due to modern lifestyle like increased age of marriage and parenting, career, stress along with environmental and modern gadgets, plastics, insecticides, smoking, tobacco and alcohol.
- The infertile couple is always in stress and demands child! Proper counseling is needed.

slump in infertility. So when the couple is demanding child, one should consider all these factors before starting major investigations.

Remember! stress is to be given on healthy lifestyle management, because—

*We Doctors are witnessing
A dramatic slump in infertility
Sperm parameters are deteriorating
Oocytes are exhausting and aging
Late marriages, late planning,
Modern gadgets, tobacco, alcohol and smoking
Plastics, insecticides, environment pollution
Junk food, adultration, mobile, internet addictions
No exercise but only stress, mentally and physically
And the chances of conceiving being wreaked
So the Lifestyle Management is to be considered!*

—Sushma Deshmukh

■ BIBLIOGRAPHY

1. Cwikel J, Gidron Y, Sheiner E. Psychological interactions with infertility among women. *Eur J Obstet Gynecol Reprod Biol.* 2004;117(2):126-31.
2. Md Hosen B, Md Islam R, Begum F, Kabir Y, Hossain Howlader MZ. Oxidative stress induced sperm DNA damage, a possible reason for male infertility. *Iran J Reprod Med.* 2015;13(9):525-32.

■ INTRODUCTION

Initial workup of an infertile couple should be very prompt and perfect. One should not delay the necessary investigations and tests. Investigations should be logical and cost effective. Special infertility file of each patient is to be maintained by the clinician.

■ DETAILED HISTORY AND PHYSICAL EXAMINATION OF THE COUPLE

Thorough history should be taken. Husband and wife should be examined completely.

Female

- *Professional history and age:* As the age advances, chances of pregnancy decreases. Career, hectic profession has a great impact on infertility.
- *Detailed menstrual history:* Age of menarche, cycle length, dysmenorrhea, oligomenorrhea, secondary amenorrhea, and gradual scanty bleeding in menstrual cycle can give certain clues like polycystic ovary syndrome (PCOS), endometriosis.
- *Duration of infertility:* Increased duration of years of infertility decrease the chances of conception and will require more evaluation.
- Coital frequency and timing and sexual history.

- *History of sexually transmitted diseases (STDs):* Chlamydia and gonorrhea can cause infertility in both men and women.
- If secondary infertility, then history of abortions/ectopic pregnancy/delivery should be taken into account.
- *If patient has received previous treatment of infertility:* Use of oral CC/Lt, total number of intrauterine insemination (IUI). If in vitro fertilization (IVF), then number of attempts, protocols used, oocyte yield, quality of embryos, fresh/frozen cycles, source of sperms/oocytes, details of embryology, and difficulties in pick up/transfer.
- *Use of previous contraceptive methods:* History of using Cu-T can suggest pelvic inflammatory disease. Oral contraceptive pills can delay the pregnancy for first 2 months.
- Past history regarding surgery (route, site), tuberculosis or any medical illness like diabetes and thyroid are very important factors in treating infertility.
- *Medications and allergies:* Some drugs affect fertility, i.e., antivertigo drugs can affect cervical mucous.
- *Family history:*
 - Family history of diabetes, hypertension in her parents. If patient having irregular menstrual cycles with obesity, then history of same problems (particularly in PCOS patients) with paternal aunt or sisters. If patient having sister, then history of marital, fertile status of her sister. If patient presented with primary amenorrhea, then in such patients, family history of such problems matters.
 - History of consanguineous marriage especially in Indian setup.
- Then detailed examination starting from weight, height, blood pressure, clinical signs of PCOS (obesity, acne, hirsutism, acanthosis nigricans), breast examination to see evidence of galactorrhea, respiratory and cardiovascular

system, abdomen, per speculum examination (to rule out genital infections, congenital malformations, cervical conditions—if needed Pap smear to be taken), and per vaginal examination.

All the important clinical findings of the patient should be noted in the separate record file.

Male

- Complete professional history/age.
- Frequency of coitus, history of tobacco chewing, smoking, alcoholism, STD.
- Any medical diseases in the past, trauma, surgery, exposure to gonadal toxins like anabolic steroids, childhood illness like mumps, developmental history (undescended testis) to be noted.
- General examination.
- Local examination to see, testis, scrotum, penis.

■ COUNSELING

- After examination, always try to counsel them together.
- If couple having previous tests, try to go through all investigations and if they are done recently then one can omit it while investigating.
- The couple is always in stress and strain. Many a times due to a long waiting period in reception, they can be irritable. Always use comfortable words. Clinician's real patience counts here only.
- Explain them everything regarding reproductive systems, fertile period by showing charts and, if possible, CD. Explain them the strategy of your treatment.
- Counseling has a very good impact on infertile couples.

■ TRANSVAGINAL SONOGRAPHY

- It is user-friendly equipment and a real friend.
- Every clinician who wants to do infertility practice should have this important asset.
- Patient can be in any phase of menstrual cycle. Try to scan the patient in first visit only.
- Transvaginal sonography not only gives information regarding uterus, ovary but also can tell you the phase of the menstrual cycle according to endometrium. See for adnexal mass, small endometrial polyps, fibroid (submucous, intramural or subserous) or any congenital anomalies. Sometimes, hydrosalpinx also can be diagnosed.
- Polycystic ovaries can be diagnosed easily by evidence of multiple follicles and dense stroma.

■ LABORATORY INVESTIGATIONS

In any infertile couple, start with the basic investigations. Basic and specialized tests will give tons of information. In females, complete blood count (CBC), urine (R), blood group and Rh, venereal disease research laboratory (VDRL), blood sugar (fasting and postmeal), serum creatinine, human immunodeficiency virus (HIV), Australia antigen, Pap smear, any specific tests according to region, e.g., sickling (which is common in central India).

In males, semen analysis, CBC, urine (R), VDRL, blood group and Rh, blood sugar (fasting and postmeal), HIV, Australia antigen and Thyroid profile.

Then detailed evaluation of the female is planned as follows.