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Infertility, Assisted Methods of Reproduction and Hormonal Assays

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Abstract

Infertility is a major public health concern in developing and developed nations. In certain societies, infertility carries a social stigma and is one of the key factors for breakup of families. The revolution created by assisted reproductive technologies (AIR) in infertility treatment has given hope to childless couples to have children. The quality of diagnosis plays an important role in helping to deliver proper therapy to such couples. Therefore, judicious use of diagnostic tests and its interpretation play a vital role in infertility treatment. The presence of andrologists and gynecologists has helped to identify and guide the patient to take proper treatment for their childlessness. Hormonal assays, its interpretation followed by hormonal stimulation, retrieval of healthy follicle, in vitro fertilization, implantation and growth of embryos require a team of experts to co-ordinate, advocate and advance the treatment to the patient. The promising field of stem cell therapy and storage banks of sperm, oocytes and embryos have opened new avenues of treatment and galvanized the field of reproduction. Therefore, books related to these aspects will help review, relate and redeem the field of infertility treatment. The ethical concerns of AIR will allow for introspection of the existing dilemmas and psychological concerns of the patient.

Keywords: reproductive health, infertility, assisted reproductive methods (AIR)

1. Introduction

“Health is defined as a state of physical, mental and social well-being of an individual, not merely the absence of disease” (WHO) [1–3].

It includes reproductive health with an ability to have a fulfilling sexual life, an inherent capacity to procreate with a freedom to make choices of timing and planning child birth. It also provides the couple the freedom to seek treatment modalities for family planning as well for infertility.

Infertility is one of the major reproductive health problems that challenge the clinicians as well as the couples. Another domain of reproductive health is the culture of a couple who apart from longing to have children face social pressures to beget children. In certain cultures, it carries social stigma as well as forms the basis for divorce bringing in the legal as well as ethical issues. The psychological domain acts negatively on fertility potential of the couple [4].

An added issue is gender bias and discrimination which falters the women as the major cause of infertility though science states that there are equal causes for infertility for both men and women [3].

2. Infertility

Infertility can be defined as the inability to conceive after one full year of regular, normal sexual intercourse without the use of any contraception. Infertility is a major health problem that affects a sizeable population in the world and the cause may be the male or female, with more or less 30–40% being due to the male factor or around 50% due to the female factor [5–7].

Oligospermia, poor semen quality, low sperm motility, anatomical defects like block in vas deferens, infections leading to inflammation of seminal vesicles, epididymis or prostate, genetic abnormalities like Klinefelter syndrome could represent major causes of male infertility [5–7].

Irregular ovulation, poor oocyte quality, blocked fallopian tubes due to infection or endometriosis are some of the causes of female infertility. Polycystic ovaries, primary and secondary amenorrhea, pelvic inflammatory disease (PID) and hostile cervical mucus may be less common causes of female infertility apart from cancer chemotherapy [6, 7].

2.1 Assisted methods of reproduction (ART)

35 years of assisted reproductive technology (ART) use has become one of the standard procedure of infertility treatment. More than 5 million babies are born after ART (1–5% births). Therefore, it is necessary to monitor, evaluate and trace the modifications of procedures with growing technical development of medical practice in the field of reproductive medicine [8].

Assisted reproduction techniques (ARTs) are defined as “all treatments or procedures that include the in vitro handling of both human oocytes and sperm or embryos for the purpose of establishing a pregnancy” [8].

2.2 Ovulation induction

Ovulation induction is useful in women with anovulatory or irregular ovulatory cycles. A hormone medication in tablet or injection form is administered to stimulate the production of follicle stimulating hormone (FSH). FSH then will help in the development of one or more follicles. Another hormone will then be administered to cause the release of ovum. The couples will be advised to have sexual intercourse during this period, creating a greater chance for conception [9].

2.3 Artificial insemination (AIH)

Artificial insemination (AIH) is also known as intrauterine insemination (IUI). AIH is recommended in cases of unknown etiology in women with healthy fallopian tubes or in men with erectile dysfunction or mechanical trauma which may hamper normal intercourse with the women. In certain cases before cancer chemotherapy or due to other reasons, semen stored in the sperm bank may be used for AIH [10].

2.4 In vitro fertilization (IVF)

In vitro fertilization (IVF) is a process in which ovum and sperm are allowed to fertilize in vitro. The process involves retrieval of ovum from the women and semen

from the male. If successful, the embryo is then implanted in the uterus of the woman using embryo transfer [11].

2.5 Gamete intra fallopian transfer (GIFT)

The ovum is retrieved from the woman and inserted between the layers of sperm and inserted into the fallopian tube. This allows natural fertilization. It is mostly used in conditions where religious beliefs do not permit IVF [11].

2.6 Intracytoplasmic sperm injection (ICSI)

Intracytoplasmic sperm injection (ICSI) is usually done in patients with oligospermia or with abnormal semen quality. It involves direct injection of single spermatozoa into the ovum to promote fertilization [12].

2.7 Zygote intrafallopian transfer (ZIFT)

Zygote intrafallopian transfer (ZIFT) involves the transfer of zygote [13].

2.8 Preimplantation genetic diagnosis (PGD)

Preimplantation genetic diagnosis (PGD) is useful in patients with a family history of genetic disorders. It may be recommended in couples with repeated miscarriages or failure in IVF or in elder patients say 35 years old or above [14].

Aneuploidy is a term used to describe an abnormality in chromosome number (fewer or more of a specific chromosome). Aneuploidy screening is performed in cases of advanced maternal age, repeated IVF failure, recurrent miscarriage and previous aneuploidy pregnancy [15].

2.9 In vitro maturation (IVM)

In vitro maturation of oocyte-cumulus complexes is a promising new technique by which immature oocytes from small follicles less than 10 mm are matured during 30–40 h in a specific culture medium. Meta-phase II (M II) oocytes with normal morphology were inseminated by ICSI [16].

3. Making a correct diagnosis

The techniques involved in infertility diagnosis include ultrasound, computerized tomography scan (CT-scan), nuclear magnetic resonance (NMR), hysteroscopy, hysterosalpingography, laparoscopy, blood karyotyping histopathology of reproductive tissues, microbiology, serology and hormone analyses [17].

For males, standard semen analyses will be carried out to assess the sperm density, motility, fertilizing ability, and detection of anti-sperm antibodies.

Computerized analyses of semen (image analyses CASA) nowadays is used for semen analyses. Therefore, poor semen quality or primary or secondary causes of infertility (hormonal imbalance at the pituitary or at the target organ level or secondary hormonal causes like thyroid dysfunction) or even obesity will help determine and evaluate the patient for IVF or ICSI procedures [18, 19].

The treatment for infertility is judiciously adopted by the treating gynecologist at different levels by initially evaluating natural menstrual history of the patient followed by advising the couple to have sexual intercourse during the ovulatory

phase. If it fails, mild ovarian stimulation with hormones will be suggested and followed by sexual intercourse. The next level of treatment may be superovulation with hormonal stimulation and retrieval of oocytes for IVF. The extra embryos or oocytes are stored for future use [19, 20].

4. Oocyte donation

Oocyte donation is one of the necessary arms of ART. It is usually recommended for women with poor ovarian reserve possibly due to primary and secondary ovarian failure. It can be due to surgical causes, damage following chemotherapy or radiotherapy, with certain genetic disorders associated with gonadal dysgenesis like Turner syndrome or patient with a known genetic disorder. It is reported that oocyte donation is one of the most successful techniques resulting in pregnancy, particularly in perimenopausal women.

One of the earlier concerns was how to *incorporate psychosocial care* into the infertility treatment protocol. This incorporation of psychosocial care is to provide the best possible care to the infertile patient. After incorporating the psychosocial care into the treatment protocol, the patient's preferences and needs are evaluated. The patient wishes to have good interaction with the staff; wishes continuity of care from the same doctor, get information that could be easily understood by the patient and to have a long standing interaction with clinic and the healthcare personnel.

Singleton pregnancies, preterm delivery and perinatal mortality as well as maternal complications, such as preeclampsia, gestational diabetes, placenta previa, placental abruption and cesarean delivery are some of the reported outcomes of ART. The following figure (**Figure 1**) explains the possible factors that may influence pregnancy outcome following ART.

Cryopreservation of oocytes and embryos involves appreciating the multiple contexts in which oocyte and embryo cryopreservation may be applied. It will enable one to understand the relative impact of cryopreservation on oocytes and embryo quality. It will allow the reader to have a grasp of the concept of selection/attrition

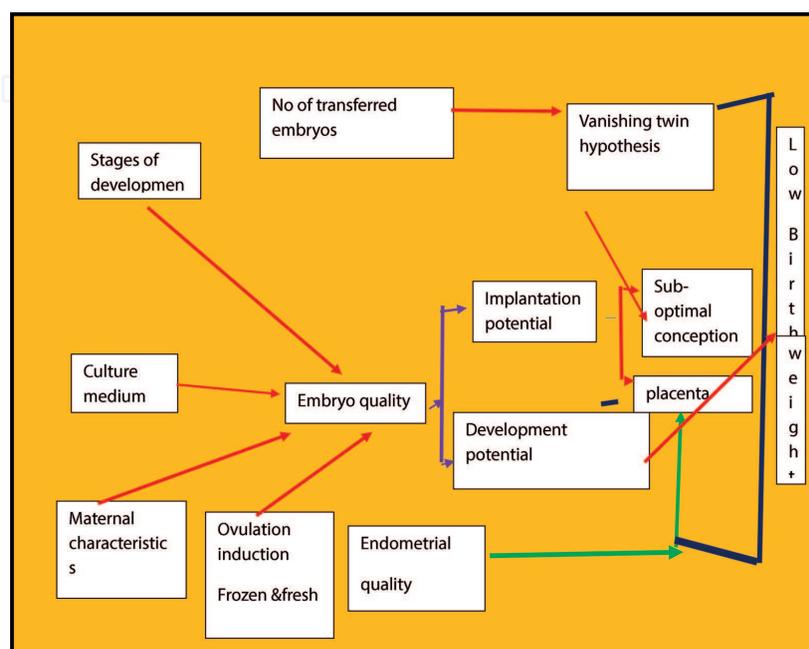


Figure 1. The factors that affect embryo/quality which determines the outcome of assisted reproductive methods.

as it applies to the efficiency of assisted methods of reproduction (ART). It will allow to gain insights into relative balance of advantages and disadvantages associated with oocyte and embryo cryopreservation in different clinical conditions.

Apart from discussions on the nature of infertility and the assisted methods of reproduction, there are widespread discussions regarding the ethical aspects related to infertile patients and ART.

Sperm banks have become one of the accessory health centers of assisted reproductive technology. In simple terms, they collect viable healthy semen samples from responsible sperm donors and preserve them according to stipulated international standards. They become the dispensing center of semen to those needy couples or couples referred to them by the physician who treat these patients. Different countries have different rules and regulations depending upon the religion and sociocultural background. Taking one aspect of a complex issue of sperm donation like keeping the anonymity of sperm donor, many countries have different opinions or regulations. Some nations want anonymous sperm donors and in some countries it is suggested that names of sperm donors be made known. In India, sperm donation is common and yet it is a social taboo, rather a social paradox—one does not want to be seen in such clinics; yet many who are desperate to have a child in the family visit these banks. In countries like India, it is said, in desperation, the recipient's father in law (husband's father or brother) comes forward to donate semen samples. What will be the sociological implications to the child born out of such donation will be an ethical issue of great concern. It is said that sperm banks are facilitators receiving semen samples from the donors and giving the samples to the needy. This sounds very pragmatic and unethical. The name sperm bank itself like gene banks dehumanizes human life and dignity. Artificial insemination (“give life and give hope” sounds like “donate blood and save lives”) may give hope to desperate parents to have children. Yet, there is lot of difference between saving lives and giving life. Giving life carries social responsibility, which needs to take into account the child's rights.

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