To Analyze the Etiopathology, Difficulty in Management and outcome in Perimenopausal Age Group Patients Attending Infertility Clinic in a Year

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Abstract

Objective: The incidence of infertility is quite increasing in India. One in every six couples is having infertility. Due to work culture, couples are planning pregnancy in their fourties. A retrospective study was conducted to analyze the etiopathology management and outcome in perimenopausal age group i.e. 44 to 55 years [1]. *Method:* This was a retrospective study conducted among 384 patients during their infertility workup, IVF, antenatal period. We reviewed the data of patients attending our clinic from Jan 2014 to Dec 2014. This was an observational study and not compared with. *Results:* The perimenopausal age group patients were 40% to 60% of the total patients. They were benefited wit IVF/ICSI with success rate of 50% to 60%. Success rate increased with donor egg upto 50% as compared to self egg (20%). 90% were caesarean deliveries. *Conclusion:* Perimenopausal age groups are a high risk group attending an infertility clinic. They are a challenge to manage, which grows as the period of gestation.

Keywords: Perimenopausal Age Group; High Risk Groups; Ageing and Infertility.

Introduction

Infertility is the inability to contribute to conception within after 12 months of unprotected intercourse [2], and it is an important public health/social taboo. Its cause could be broadly divided into three groups female, male and unexplained factors. The female factors include problem with the ovulation due to obesity or polycystic ovarian changes, or due to erratic level of progesterone, due to pre-LH surge in the mid-luteal phase, or due to adhesion problems from pelvic inflammatory disease, tubal obstruction due to tuberculosis and endometriosis, or due to unidentified cervical factors [3].

The need for fertility at midlife is on the rise due to delayed childbearing especially in career-oriented women, who may be either having late marriages or planning childbearing after they have stabilized in their careers. Increased rate of divorce with remarriage also adds to the number of women who opt for fertility beyond the age of 40.

It is proven from a number of studies that with age, there is a natural decline in fertility due to the decreasing quantity as well as quality of the ovarian follicles.

Age has a detrimental effect on the quality of the oocytes. Studies have shown that the rate of aneuploidy is low in women less than age 35 years (10%), but increases to 30% at the age of 40 years, to 40% at the age of 43 years and to 100% in women more than age 44 years [4].

One of the preventable cause of infertility in the couple is sexually transmitted diseases (STDs) particularly chlamydia and gonorrhea if untreated. They cause infertility by damaging the tubes, by altering their physiology and anatomy. The incidence of infertility increases with the incidence of PID.

In India, one of the most important reasons for declining fertility in women is

due to tubercular infection, leading to tubal, endometrial and other reasons for declining fertility. Genital tuberculosis (TB) affects the fallopian tube more commonly, and in 50% of the cases endometrium is also involved. Incidence of infertility in genital TB varied from 10% to 85%.

Smoking in women also leads to problems of conception, miscarriages and intrauterine fetal growth retardation (IUGR). The extent of damage depends on the quantity and duration of smoking. Nicotine causes irreversible damage. Alcohol consumption in women also leads to longer time in conception and more miscarriages and fetal alcohol syndrome.

Increasing prevalence of polycystic ovarian syndrome (PCOS) is a contributor in the increasing incidence of infertility. PCOS is a lifestyle related disease. As there is increase in trend of sedantry lifestyle, increased BMI, hyperglycemia due to faulty eating habits, all adds to pathophysiology of PCOS.

Endometriosis leads to anatomical distortions leading to infertility and adhesions. Other causes of infertility are, Asherman's syndrome, cervical factors, immunological and unexplained factors.

Material and Method

We retrospectively reviewed all patients who underwent IVF cycles in our institution from Jan 2014 to Dec 2014. We selected patients within age group 44 to 55 years. We used long protocol for controlled ovarian hyper-stimulation. In the long agonist protocol, pituitary desensitization with daily SC administration of 1mg leuprolideacetate began in the mid luteal phase of the previous menstrual cycle. This dose was continued until ovarian quiescence was confirmed by ultrasound examination in next menstruation and estradiol value less than 30pg/ml, after which the dose of leuprolide was halved and stimulation with recombinant FSH was started until the day of HCG injection. Doses were adjusted according to the response seen on TVS examination. Human chorionic gonadotropin was administered subcutaneously when at least two leading follicles reached a mean diameter of 18mm. Trans vaginal oocyte retrieval was scheduled 34 to 36 hours after HCG injection. Embryo transfer was performed 2 - 3 or 5 - 6 days after oocyte retrieval via the vaginal route. Patient was called 15 days after transfer for serum beta HCG, after beta HCG positive, sonographic documentation of pregnancy was being done after 1 week.

During antenatal visit, patient was examined periodically clinically as well as with sonography. A thorough history was taken. A record of blood pressure, weight, fundal height, abdominal girth was made at each visit supplemented with sonography. After 7 months, color Doppler was being done fortnightly. In most of the cases, elective termination of pregnancy by cesarean section done due to various factors complicating pregnancy. Patient remain admitted in hospital for three days and baby was shifted to NICU, if needed.

Results

Out of 962 patients, 384 were in the perimenopausal age group which is 40% of total patients. Total 336 patients were in age group of 44 to 49 years and 48 were in age group of 50 to 55 years, as

Table 1:

Age group	Total patients	Percentage
All age Groups	962	100%
44 – 49 years	336	35%
50 – 55 years	48	5%

shown in the Table 1.

Out of these, 312 i.e. 81.25% were premenopausal and 72 were postmenopausal i.e. 18.75%.

The causes of infertility were studied in detail and established clinically and corroborated with laboratory evidence, diagnostic laparoscopy and hysteroscopy.
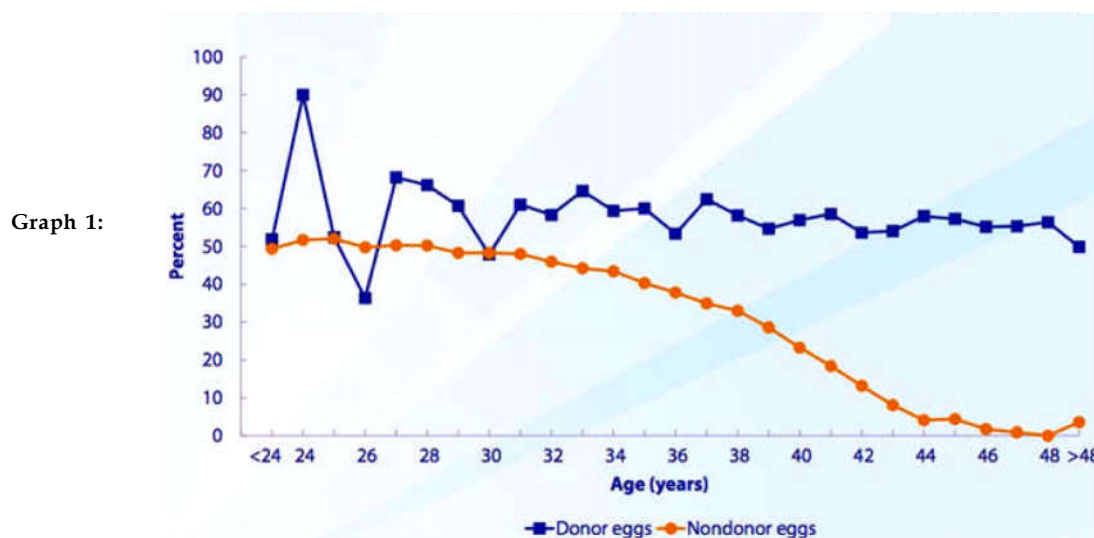
Table 2:

Factors	%
Tubal factor + low OR	59
Ashermen syndrome	9
Multiple fibroids	7
Adenomyosis	5
Endiometriosis	5
Male factor	15

Etiopathological factors governing the infertility are as shown in the Table 2.

We can clearly depict out that tubal factor plus low ovarian reserve was the main cause of infertility in 59% of cases, which is a significant number.

Those patients, having tubal factors plus low ovarian reserve with male factor infertility were banifited with IVF/ICSI offering 50% to 60% success rate. As with age, quality of eggs deteriorate, sosuccess

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Percentage of Transfers using Fresh Embryos from Donor or Non Doner Eggs

Graph 1:

rate with self-egg was 20% to 30% only, at the same time, success rate with donor egg was 50% to 60%. As shown in the Graph 1.

Patients have almost 70% incidence of threatened abortion even with good hormonal support. Persistent vaginal bleeding with ongoing pregnancy was reported in 20% to 30% of patients. Chronic hypertension was reported in 20% of patients with superimposed gestational hypertension of 15%. The total incidence of hypertension were 35%. The common ailments of pregnancy were seen in 70% of patients, with 30% to 40% having them throughout the pregnancy. 70% were having GI problems like constipation during pregnancy. Hypothyroidism was reported in 58% patients. Type 2 diabetes with superimposed gestational diabetes was noticed in 35% patients.

Average AFI at 30 weeks of gestation was 8cm to 10cm, at 36 weeks average AFI was 5cm to 6cm. 85% of newborns were having low birth weight and required NICU services. Out of these, 36% of babies were appropriate for gestational age, i.e. pre-term, 55% were IUGR. Average baby weight was 1.8kg to 2.2kg at 34 to 36 weeks of gestation.

Average POG at termination of pregnancy was 34 to 36 weeks in 50% patients, it was before 34 weeks in 15% patients and 35% at 36 weeks. Mode of termination of pregnancy was LSCS in 90% cases. Intraperitoneal adhesions were reported in 20% cases, 40% to 60% were having adherent placenta. Moderate to severe PPH was reported in 20% patients with 2% needed peripartum hysterectomy.

Recovery in puerperium was slow. There was increased incidence of subinvolution and secondary PPH in 5% of the cases. Lactational failure and postpartum depression was reported in 50% to 60% patients.

Discussion

The quality of oocyte and embryo are important determinant in success of IVF. With age, there is a natural decline in fertility due to the decreasing quantity of the ovarian follicle [5]. As shown in Graph 2.
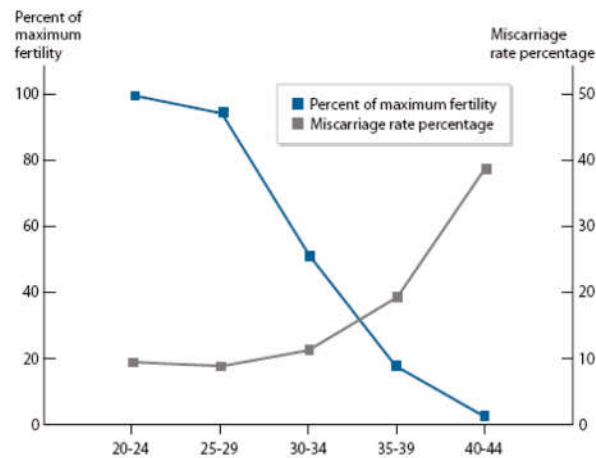
Graph 2:

Age as an ovarian function marker was found to have prognostic value in general infertile population because age showed strong correlation with all the markers of ovarian functions like AMH, AFC, E_2, inhibin and FSH. AMH better correlated with the decreasing pool of follicle with age than the other markers. It appears to be the best marker of gradual dwindling of follicle numbers and ovarian volume as it is a time independent marker. Its value does not

vary with the day of cycle [7].

The increased population of perimenopausal age group is due to increased awareness, increased social acceptance of IVF, reduction in cost of treatment, promising results, good antenatal care and improved NICU care.

Various protocols for ovulation induction during assisted reproduction technology have been utilized to improve pregnancy rates in perimenopausal women with no concrete evidence available on the most ideal protocol to use. Currently, the most common in practice is long protocol with remarkable success in our institution.

Currently, in women who do not show good ovulation pattern on maximal ovarian stimulation, or in those who have repetitive failed ART cycles with their own eggs, use of donor oocytes gives the best results. Data from the American Society of Reproductive Medicine shows a pregnancy rate of 46.6% in women less than 35 years of age and a pregnancy rate of only 19.5% above the age of 40 years after assisted reproduction in fresh embryo cycles. On the other hand in women who adopted donor oocytes, the pregnancy rate was 56.6% at the age of 40 years [8].

We could not find a study with which we compare our results. Pregnancy in perimenopausal age group constitutes a high risk group in terms of antenatal, intrapartum, postnatal and neonatal management [9]. They need a lot of antenatal visits in comparison to younger age group. The common ailments of pregnancy are increased in these patients due to anxiety, previous infertility, BOH in some cases and due to precious pregnancy. Endocrine disorders like hypothyroidism and diabetes carries separate risks for successful pregnancy. The overall incidence of hypertension complicating pregnancy is increased due to equal incidence of chronic as well as gestational hypertension [10].

Factors complicating the placenta like placenta previa, adherent placenta, placental calcification, poor placentation are common. IUGR is increased due to medical complications and oligohydramnios wit average AFI in the lower normal range.

The incidence of cesarean deliveries increases in these patients, the indications being preterm PROM, IUGR, oligohydramnios, NPOL.

The termination of pregnancy in these patients is required earlier than the term. The intra op difficulties like intraperitoneal adhesions, adherent placenta, fibrosed uterus are commonly seen. Due to atonicity of uterus and adherent placenta, incidence of PPH increases.

Postpartum depression, lactation failure and secondary PPH have more chances to occur in such patients.

Conclusion

40% to 60% of total patients attending infertility clinics were in perimenopousal age group. Tubal factor plus low ovarian reserve was the major cause of infertility. IVF/ICSI offers a good success rate. Success rate was more with donor egg than with self-egg. Perimenopausal age pregnancy is a high risk pregnancy in terms of antenatal, intrapartum, postnatal and neonatal management. It requires great expertise and it overburdens the healthcare provider in terms of number of visits.

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