

## **Antral Follicle Count as Predictor of Ovarian Reserve**

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Infertility is the inability to conceive following 1 year of unprotected intercourse in cases where the female is  $\leq$ 35 years of age or following 6 months of unprotected intercourse for women >35 years of age. The female factor infertility is found in 40% of cases, the male in 20% of cases and the both male and female factors in 20% of cases. Female factors can further be divided into tubal (40%), ovulatory (40%), uterine (10%) and cervical (10%). The spontaneous conception rate for the "normal" couple has been found to be 25% per ovulatory cycle.

As the major causes of infertility are ovulation dysfunction and fallopian tube obstruction, the preliminary investigations for the infertile couple should be focused on detection of ovarian function by hormonal assay (early follicular FSH and LH levels, and mid-luteal progesterone), and evaluation of tubal patency by hysterosalpingography [1].

## **1. OVARIAN RESERVE (OR)**

The primary function of the ovary in a woman is the production of a mature and viable oocyte which is capable of fertilization and undergo subsequent embryo development and implantation. At birth, the ovary contains a finite number of oocytes available for folliculogenesis. This finite number of available oocytes is termed "the ovarian reserve". The determination of ovarian reserve is important in the assessment and treatment of infertility. As the ovary ages, the ovarian reserve also declines. Ovarian reserve (OR) refers to the number and quality of oocytes that, at any given age, are available to produce a dominant follicle late in the follicular phase of the menstrual cycle. By estimating the OR, one may predict the remaining reproductive lifetime as well as the success of assisted reproductive likelv techniques (ART) such as in vitro fertilization

For the general practitioner performing an infertility evaluation, focus is recommended on

(IVF) [2].

the following groups of women for ovarian reserve testing:

- Women over 30 years of age
- Women with a history of exposure to a confirmed gonadotoxin, i.e., tobacco smoke, chemotherapy, radiation therapy
- Women with a strong family history of early menopause or premature ovarian failure
- Women who have had extensive ovarian surgery, i.e. cystectomy and unilateral oophorectomy.

The tests to evaluate the ovarian reserve may be divided into static markers- measured during the early follicular phase (estradiol, folliclestimulating hormone, inhibin-B, and anti-Müllerian hormone), dynamic markers (tests of stimulation with clomiphene citrate. gonadotropins and gonadotropin releasing hormone analogues), and sonographic markers (antral follicle count and ovarian volume). These tests are used primarily to assess treatment prognosis in infertile women. In time to come, the population may be screened to assess ovarian reserve so as to provide many more women with information about their reproductive potential and help them shape their life plan.

## 2. ANTRAL FOLLICLE COUNT (AFC)

There is no consensus on identification of the antral follicles. However, several evidence based studies have suggested to select the follicles as antral follicles based on a diameter of 2 to 10 mm [3, 4]. Thus, the antral follicle count (AFC) is defined as the number of follicles smaller than 10 mm in diameter detected by Transvaginal Ultrasound (TVUS) in the early follicular phase. As a direct marker of the cohort of growing follicles in the early menstrual cycle, the AFC is believed to correlate strongly with the number of primordial follicles present in the ovary and, thus, the

ovarian reserve. Total AFC of less than 5 to 10 is suggestive of diminished ovarian reserve [5]. There is no significant difference between right-sided and left sided antral follicle counts within the same individual [6].

In one study, a number of ovarian reserve tests were performed, such as AFC and an endocrine test panel on sub-fertile, ovulatory patients [7]. The study demonstrated that the number of preantral or small antral follicles (2–6 mm) declined with age and the number of larger follicles (7–10 mm) remained constant, suggesting that the number of small AFCs represents the functional OR [7].

The effect of age on AFC has remained interesting. Scheffer et al. [8] reported a biphasic pattern of AFC decline in their population as AFC declined by 4.8% per year before the age of 37 years, compared with 11.7% after this threshold. On a second analysis on the same dataset, a model with linear decline in AFC until the age of 43 years followed by an exponential decline with asymptote at zero was used to describe the data [9]. The conventional linear model gave the best fit to the AFC in all other studies investigating the relationship between age and AFC [10].

The age-related decline in female reproductive function owing to the reduction of the ovarian follicle pool and the quality of oocytes has been well established. A reliable marker for the age at which subfertility will occur would have great potential value as a predictor of future reproductive life span. As a large proportion of female subfertility arises from postponed childbearing, any reliable measurement of ovarian reserve may also be of interest to women in general. Hence the assessment of ovarian reserve to determine the strategy for treatment of female subfertility or infertility has become essential.

Traditionally, age, follicle stimulating hormone (FSH) & estradiol (E2) levels and antral follicle count (AFC) on ultrasound investigation in the early follicular phase have been used for evaluation of ovarian reserve. However, the FSH level has been found to be above the norm with largely decreased ovarian function [11]. The AFC has been found to predict poor response much efficiently than basal FSH [12].

Measurement of anti-Mullerian hormone (AMH) levels has also become important in assessment of ovarian reserve. In comparison to other ovarian reserve assessment tests, AMH is characterized by a number of advantages. AMH levels are stable throughout the menstrual cycle and so can be measured at any day of the cycle [13, 14]. Moreover, AMH levels are not affected by other hormonal variations, including the use of oral contraceptives [15]. However, a recent study by Bentzen et al. has indicated that ovarian reserve markers are lower in women who use sex steroids for contraception [16]. Thus, AMH concentration and AFC may not be that accurate as predictors of ovarian reserve in women who use hormonal contraception.

Unfortunately, the studies concerning physio logical ovarian aging in women with and without fertility problems are very limited and most of them are done in Western countries. Therefore, it is high time that evaluation of aforementioned ovarian reserve test parameters is also done in women of different ages in Indian population.

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