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" YTP UPDATE 2020"

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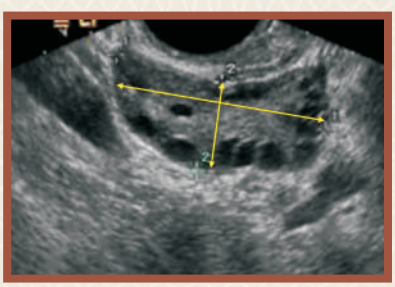
Investigations on Day 2 of IVF Cycle

Day 2 investigations are conducted on day 2 of period and includes Baseline Ultrasound Scan, Antral Follicle Count (AFC), Serum Estradiol (E2), Follicle Stimulating Hrmone (FSH), Luteinizing Hormone (LH) and Progesterone (P4). These help to predict ovarian response. In the process of Controlled Ovarian Hyperstimulation (COH), the principle steps are to evaluate ovarian reserve function, predict ovarian response, and develop an optimal individualized COH protocol.

Baseline scan should be trans-vaginal for higher accuracy. This scan is done on 2nd or 3rd day of the cycle. At this time of the cycle, the ovaries have no active follicles; estrogen and progesterone are both at lowest levels, endometrium is thin like a single line, as it has shed off during menstruation. It is done to classify the ovaries in one of the three categories: 1. Polycystic Ovaries, 2. Normal Ovaries, 3. Low Reserve Ovaries. A normal ovary has the following reference values:

1. Diameter 2-3.5 cm
2. Volume 3-6.6 cc
3. Stromal RI 0.6-0.7
4. Stromal PSV 5-10 cm/sec
5. Follicle no per ovary (FNPO) 5-12

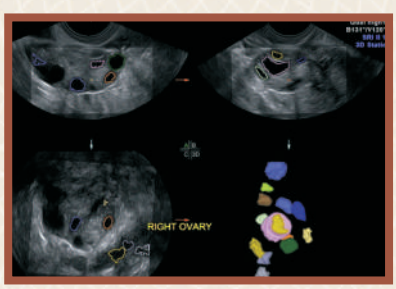


AFC (Antral Follicle Count) :

The AFC indicates the number of follicles with diameters of 2mm to 9mm. They begin to develop after recruitment in the luteal phase of the previous cycle and reflect the number of follicles that will continue to mature during the ovulation treatment cycle.

Counting ovarian antral follicles by ultrasound: AFC should be performed with the help of a transvaginal ultrasound (US) probe with frequency ≥7MHz. AFC is assessed by using real-time two-dimensional (2D) US, stored 2D-US cine-loops and stored three-dimensional (3D) US datasets. Real-time 2D-US is advantageous as it permits additional maneuvers to determine whether an anechoic structure is a follicle, but requires a longer scanning time, especially when there are large number off ollicles, resulting in more discomfort to the patient. 2D-US cine-loops have reduced scanning time and the possibility for other observers to perform the count.

The antral follicles become identifiable by US more easily when they reach 2mm in diameter, coinciding with higher sensitivity to FSH. Antral follicles measuring between 2 and 10mm are 'recruitable', while antral follicles >10mm are usually referred to as 'dominant' follicles. It is believed by some that the number of follicles measuring only up to 5-6mm represents the best cohort of recruitable follicles and correlates better with the true ovarian reserve however, distinguishing follicles that measure 5-6mm from those measuring 7-9mm may increase the time needed to count without any clinical benefit.



Follicle Stimulating Hormone (FSH)

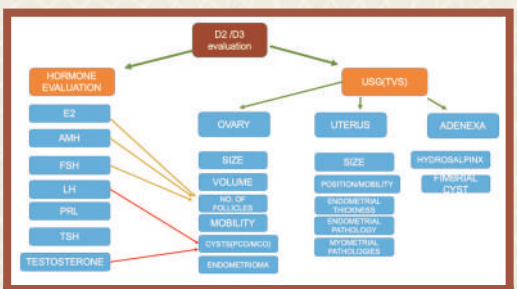
Early follicular phase serum FSH is the commonly used endocrine test for determining the ovarian reserve. It is based on the feedback inhibition of FSH secretion by ovarian hormones and is an indirect marker of the ovarian reserve. At the beginning of the menstrual cycle, the estradiol (E2) and inhibin B levels inhibit FSH secretion from the pituitary. In women with diminished ovarian reserve, the production of ovarian hormones is insufficient, and this leads to elevated pituitary FSH secretion. Levels of FSH higher than 9 IU show a decreased ovarian reserve.

Luteinizing Hormone (LH)

Day 2 LH should ideally be below 5IU/l. The levels show down regulation when less than 2 IU/l. There may be raised levels in case of PCOS.

Estradiol (E2)

For IVF cycle E2 is done on day 2. If E2 > 80 pg/ml, it indicates poor IVF outcome as it indicates early follicular recruitment due to high FSH and poor ovarian reserve. Raised E2 on day 2 may also be present in case of a basal cyst and stimulation should be shifted to next cycle. E2 levels are a reflection of the ovarian response. Early elevations in basal serum E2 are due to the advanced follicular development and the early selection of a dominant follicle, as seen in older women, due to rising FSH levels. It has been observed that women with E2 levels <20 pg/ml or ≥80 pg/ml have a higher artificial reproductive techniques (ART) cycle cancellation rate. Combining E2 with FSH on cycle day 3 is shown to have reduced the incidence of false-negative tests obtained when FSH alone was used. The elevation of both indicates poor ovarian response. E2, however, has low predictive accuracy and lacks high sensitivity and specificity cut-off levels. It may be used as a guide for starting stimulation with gonadotropins; however, it should not be used to exclude couples from ART program.



Flowchart (by Dr Amogh Chimote)

Progesterone (P4)

Progesterone levels refer to the measurement of ovarian function. Progesterone levels are low during the follicular phase (<1 ng/ml), rise on the day luteinizing hormone (LH) surges (1–2 ng/ml), and increase until they peak approximately 1 week after ovulation. The levels <3 ng/ml imply anovulation, except when evaluated after a woman ovulates or prior to menses when progesterone levels are at a physiological low. Raised early follicular phase progesterone levels in menstrual cycle indicates an inefficient luteolysis. If progesterone is more than 1.5 ng/ml stimulation should be postponed as it is indicative of a basal cyst or an active corpus luteum.

Proposed protocol for Ovarian Reserve (OR) screening :

- Ovarian reserve screening should be provided to all women at 30 years of age who potentially seek future fertility and should be voluntary.
- Pre-screening counseling regarding the decline in fertility with age and merits/de-merits of ovarian reserve screening must be performed before the test is ordered.
- AMH is an ideal screening test of ovarian reserve as it is the least expensive and intrusive, has the least inter-observer variability and can be taken at any stage in the menstrual cycle.
- AMH result below the 10th percentile for age indicates that the individual has poor ovarian reserve.

Conclusion :

Hormonal and TVS evaluation both are essential. Maintaining a balance and correlation gives the best outcome