

COMPARISON OF SERUM FOLLICLE STIMULATING HORMONE (FSH) LEVELS, ESTRADIOL 2 (E2) LEVELS, ANTI MULLERIAN HORMONE (AMH) LEVELS FOR ASSESSING THE OVARIAN RESERVE IN FERTILE & INFERTILE WOMEN

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ABSTRACT:

Background: Since the quantity & quality of ovarian reserve decreases with age, Serum Anti Mullerian Hormone (AMH) levels might be useful in predicting ovarian aging. **Aims & Objectives-** To compare the Follicle stimulating hormone (FSH) levels, Estradiol 2 (E2) levels, AMH levels in fertile & infertile women & find their correlation with ovarian reserve. **Material & Methods:** This prospective cross-sectional study was conducted in the Department of Obstetrics & Gynaecology of our Tertiary care hospital from June 2015 till December 2015. The study recruited 30 fertile women (Group F) and 30 infertile women (Group I) in the age range 26 to 36 yrs. The subjects with regular menstruation with a cycle length of 28-35 days were included in the study. 3 ml of intravenous blood was taken from study subjects and sent to laboratory for biochemical estimation of FSH, E 2 on day 3 and AMH. A trans vaginal ultrasonogram was conducted to measure ovarian volume and the antral follicular count. **Results :** In Group I, the study subjects presented with statistically significantly elevated FSH levels, low AMH levels and low ovarian volumes and AFCs than Group F. The AFC, ovarian volume, AMH negatively correlated with age ($r=-0.56$, $p<0.05$). The ovarian volume, AMH positively correlated with the AFC ($r=0.637$, $p<0.05$). While FSH negatively correlated with the AFC ($r= -0.134$, $p<0.05$). **Conclusion:** The study observed reduction in the serum antimullerin hormone levels which correlated with the ovarian volume & antral follicular count. Thus, serum antimullerin hormone levels can be used as novel marker to assess the ovarian reserve.

Keywords- Antimullerin hormone, ovarian reserve, FSH

INTRODUCTION:

Infertility is a social taboo, in India, affecting around 6.9-9.3% of the females. Ovarian Reserve refers to the functional ability of the ovary & reflects the number and the quality of the oocytes present. (1) The quality & quantity of the oocytes declines with an increasing age. Various serum markers are being used to assess the ovarian reserve like FSH, E2, inhibin B, AMH & antral follicle count (AFC). (2) Various studies have been conducted on the infertile women assessing

the correlation between ovarian reserve & pregnancy outcomes. (3,4) Researches suggest that ovarian reserve reflects only quantity and not the quality of remaining oocytes. Also, ovarian reserve is a poor predictor of conception where assisted reproductive techniques are used. (5) Some studies, have correlated high FSH levels as a marker of low ovarian reserve, & found it to be associated with a longer time to spontaneous pregnancy regardless of age,

increase in miscarriage and early menopause.(6) Since, varying data is available on ovarian aging, FSH levels & AMH levels & pregnancy outcomes. Van MJM et al 2004 conducted a prospective study that failed to find an association between FSH and pregnancy outcome. (7) Thus, this study was conducted to compare the FSH levels, E2 levels, AMH levels in fertile & infertile women & find their correlation with ovarian reserve.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted in the Department of Obstetrics & Gynaecology of our Tertiary care hospital from June 2015 till December 2015. The study recruited 30 fertile women (Group F) and 30 infertile women (Group I) in the age range 26 to 36 yrs. The subjects with regular menstruation with a cycle length of 28-35 days were included in the study. A prior institutional ethical clearance was sought and written informed consent taken from the study subjects. Subjects with thyroid illness, Diabetes mellitus, PCOS, history of ovarian surgery & male partner infertility excluded.

3 ml of intravenous blood was taken from study subjects and sent to laboratory for biochemical estimation of FSH, E2 on day 3 and AMH. A trans vaginal ultrasonogram was conducted to measure ovarian volume and the antral follicular count.

Statistical analysis

The collected data was tabulated in excel spread sheet put to statistical analysis. The data was expressed as mean and standard deviation. P value at 0.05 was considered statistically significant. A spearman correlation test was

conducted to find the correlation between different parameters.

RESULTS

In Group I, the study subjects presented with statistically significantly elevated FSH levels, low AMH levels and low ovarian volumes and AFCs than Group F.

The AFC, ovarian volume, AMH negatively correlated with age ($r=-0.56$, $p=0.001$). The ovarian volume, AMH positively correlated with the AFC ($r=0.637$, $p<0.05$). While FSH negatively correlated with the AFC ($r= -0.134$, $p<0.05$). (Table 1)

Table 1 shows the levels of various parameters in Group I & Group F

	Group I	Group F	P value
Age	32±2.61	29.63	<0.05
BMI	24.56±1.45	23.45±1.04	>0.05
Ovarian reserve	9.38±2.75	11.2±3.69	<0.05
AFC	6.8±3.2	9.3±3.92	<0.05
FSH	9.4±4.2	7.24±2.6	<0.05
E2	163±69	140±58	>0.05
AMH	2.89±0.94	3.7±1.24	<0.05

DISCUSSION

In the present study, elevated serum FSH levels were observed in infertile women than fertile women which was statistically significant ($p<0.05$). The levels of FSH increase with increase in follicular age & its fluctuation during cycle makes the ovarian reserve estimation difficult. (8) Rise in FSH levels are considered to indicate reduction in ovarian reserve & increase on day 3 is noted to be a late marker of decreased fertility.(9) Similarly , Agarwal A 2014 study stated day 3 FSH levels correlated well with the

chronological age & suggested it to be a marker of ovarian reserve. Raised basal oestradiol level is a poor predictor of ovarian reserve, even when the basal level is normal. Thus, the oestradiol levels at day 3 prediction of the ovarian reserve are questionable & which is why AFC & AMH values should be considered important. (8)

In the present study, reduced AFCs were observed in infertile women than fertile women which was statistically significant ($p < 0.05$) Similarly, study by Rosen MP et al 2011 stated that reduced AFC count have been observed in infertile women which suggest that factors that affect the size of the remaining follicle pool, also affect oocyte quality and the likelihood of conception (2). Similarly, Agarwal A 2014 study stated AFC levels correlated well with the age (8).

AFC is an essential tool & an indirect measurement of the ovarian reserve. It is considered superior to the basal oestradiol level in the prediction of a poor ovarian response. The AFC visualization requires a 3D ultra sonogram with trained professionals. (10)

In the present study, ovarian volume showed a low value which correlated with the number of growing follicles. The size, shape and activity of human ovaries changes throughout life. A study conducted by Pavlik F et al 2000 observed a relationship between ovarian volume & age. (11) It showed a statistically significant decrease in the ovarian volume with each decade of life, from 30 to 70 years. Study by Erdem M 2003 on fertile and infertile women in age range 35-45 years, a negative correlation was observed between the mean ovarian volume and age. (12)

In the present study, with advancing age, serum AMH levels decreased. In Infertile women, serum AMH levels were statistically

significantly lower than fertile women. A positive correlation was observed between AMH with the AFC and the ovarian volume. Accordingly, studies conducted by V. S Kalaiselvi et al 2012 observed the same results (10).

The mean serum AMH levels in a women aged 35 yrs is found to be 2.0ng/ml. Serum AMH levels less than 1.0ng/ml indicates a reduced ovarian reserve, especially when it is associated with a low AFC (13, 14). AMH is secreted by the granulosa cells of the recruited follicles. It acts as regulator of the recruitment & prevents the depletion of all the primordial follicle pools. It is considered a better predictor of the ovarian response (14). It can be tested both in the follicular as well as the luteal phases since it is independent of the cycle (15). Its sampling technique is easier compared to the ovarian volume and the AFC, which involves usage of 3D ultrasonogram and specialists. Thus, AMH should be assessed as a useful marker for the assessment of ovarian reserve in future. Further, extensive studies should be done in order to it be routinely used.

CONCLUSION

The present study concludes antimullerin hormone significantly correlates with the ovarian reserve and can be considered a potential marker for assessing the ovarian follicular pool in the ovary. Future research endeavors should focus on validating AMH as a routine marker for ovarian reserve assessment and exploring its utility in clinical practice. Additionally, comprehensive studies are warranted to elucidate the intricate mechanisms underlying ovarian aging and its implications on fertility outcomes.

REFERENCES

1. Te Velde ER, Pearson PL. The variability of female reproductive ageing. *Hum Reprod Update*. 2002; 8: 141 – 54.
2. Rosen MP, Johnstone E, Addaun-Andersen C, Cedars MI. A lower antral follicle count is associated with infertility. *Fertil Steril*. 2011 May;95(6):1950-4, 1954.e1. doi: 10.1016/j.fertnstert.2011.01.151. Epub 2011 Mar 3.
3. Visser JA, De Jong FH, Laven JS, Themmen AP. Anti Mullerian Hormone: A new marker of ovarian function. *Reproduction*. 2006;131: 1-9.
4. Feyereisen E, Mendez Lozano DH, Taieb J, Hesters L, Frydman R, Fanchin R. Anti-Mullerian hormone: clinical insights into a promising marker of ovarian follicular status. *Reprod Biomed Online*. 2006; 12: 695 – 703.
5. Jirge PR. Ovarian reserve tests. *J Hum Reprod Sci*. 2011 Sep;4(3):108-13. doi: 10.4103/0974-1208.92283.
6. Kok HS, van Asselt KM, van der Schouw YT, Grobbee DE, te Velde ER, Pearson PL, et al. Subfertility reflects accelerated ovarian ageing. *Hum Reprod*. 2003;18(3):644–8.
7. van Montfrans JM, van Hooff MH, Huirne JA, Tanahatue SJ, Sadrezadeh S, Martens F, et al. Basal FSH concentrations as a marker of ovarian ageing are not related to pregnancy outcome in a general population of women over 30 years. *Hum Reprod*. 2004;19(2):430–4.
8. Abha Maheswari, Paul Fowler, Siladitya Battacharya. Assessment of ovarian reserve-should we perform routinely? *Human Reprod*. 2006; 21: P 2729-35.
9. Perloe M., Levy DP, Sills ES Strategies for ascertaining ovarian reserve among women suspected of subfertility. *Int J Fertil Womens Med*. 2000; 45, 215-24.
10. Kalaiselvi VS, P S, K P, Krishna G P. The anti mullerian hormone- a novel marker for assessing the ovarian reserve in women with regular menstrual cycles. *J Clin Diagn Res*. 2012Dec;6(10):1636-9.
11. Pavlik F, De Priest PD, Gallion Hh, Ueland FR, Reedy MB, Kryscio RJ et al. Ovarian volume related to age. *Gynecol Oncol*.2000; 77: 410-12.
12. Erdem M, Erdem A, Biberoglu K, Arslan M. Age related changes in ovarian volume, antral follicle counts and basal follicle stimulating hormone levels comparison between fertile and infertile women. *Gynecol, Endocrinol*. 2003; 17:199-205.
13. VanRooji IA, Broekmans FJ, te Velde ER, Fauser BC, Bancsi LF, de Jong et al. Serum anti-Mullerian hormone levels: a novel measure of ovarian reserve. *Hum Reprod*.2002; 17: 3065 – 71.
14. Nelson SM, Yates RW, Lyall H, Jamieson M, Traynor I, Gaudoin M, Mitchell P, Ambrose P, Fleming F. Anti-mullerian hormone-based approach to controlled ovarian stimulation for assisted conception. *Human Reprod*. 2009; 24: 867-75.
15. La Marca, Volpe A. Anti Mullerian Hormone in female reproduction is measurement of circulating AMH a useful tool? *Clin Endocrinol*. 2006 ;64: 603-10