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Does AMH And FSH Predict Ovarian Reserve And Chance Of Sucessful Pregnancy?

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Abstract:
Background:
Societal and behavioral shifts in recent years have resulted in a trend towards delayed child bearing which has lead to increase in infertility from 6% in women aged between 15-24 years to Less than 30% in the age group of 35 -44 yrs old .This has created a demand from patients & clinicians for a method to monitor fertility.
Study Objective:*To evaluate the role of Anti mullerian hormone (AMH) also known as Mullerian inhibiting Substance (MIS) and follicle stimulating hormone (FSH) as potential markers in monitoring the fertility in patients with assisted reproduction. It is a retrospective study done at KIMS hospital.*
Results: *In the present study AMH had a significantly positive correlation with IVF outcome, the (r) value was 0.529 at a 2 tailed significance of < 0.001. When compared to FSH, had a significantly negative correlation with IVF outcome, r value -0.445 at a 2 tailed significance of p< 0.002. ROC curve analysis showed AMH was 83.3% sensitive and 77.3% specific at a best out off value of 18.5pM and FSH was 68.2% sensitive and 87.5% specific at a best cutoff of 10.15 mIU/ml, in assessing the outcome of IVF. It was also observed that AMH has a positive predictive value of 80.7% and negative predictive value of 88% on comparison FSH has a positive predictive value of 75% and negative predictive value of 83%.*
Conclusion:*Thus AMH can be considered as a convenient and useful measure of assessing ovarian reserve. AMH and FSH tests thus measure the ovarian reserve and are useful tools for predicting the ovulation induction response*
Keywords: *AMH, FSH, Infertility in Females, IVF.*

I. Background

Societal and behavioral shifts in recent years have resulted in a trend towards delayed child bearing which has lead to increase in infertility from 6% in women aged between 15-24 years to Less than 30% in the age group of 35 -44 yrs old .This has created a demand from patients & clinicians for a method to monitor fertility. We evaluated the role of Anti mullerian hormone (AMH) also known as Mullerian inhibiting Substance (MIS) and follicle stimulating hormone (FSH) as potential markers in monitoring the fertility in patients with assisted reproduction.

AMH in produced in small amounts exclusively by the ovarian granulosa cells and becomes undetectable by menopause. Its concentration is directly related to the actual follicle count indicating ovarian function[2]. In the previous studies it was demonstrated that AMH continues to be produced by the granulosa cells of early growing follicles and continues to be produced until the early antral stage where upon it declines precipitously. It therefore helps in reflecting the size of growing follicle and thus by implication the number of primordial follicles. As the recruitable pool represents a constantly cycling population of follicles, peripherally detectable AMH remains relatively stable with in and between the menstrual cycles[3].

FSH also stimulates the growth and functioning of gonads. In women the gonadotrophins act with in the hypothalamic-pituitary-ovarian axis regulating circuit to control the menstrual cycle[4].

FSH is released in pulses from the gonadotrophic cells of the anterior pituitary; together with LH it stimulates the growth and maturation of follicle[5]. Measurement of serum FSH levels at 2-3 days after the onset of full menstrual flow has been shown as a marker of ovarian reserve. Over all low levels of FSH during early follicular phase reflects the normal hypothalamic- pituitary- ovarian- uterus axis. Premature rise in FSH suggests shorter follicular phase[1].

As AMH and FSH are known markers reflecting the ovarian function, in the present study we there fore aim to evaluate the role of AMH and FSH in assisted reproductive technology and compare their roles in predicting the ovarian response and chance of successful pregnancy in women opting for assisted reproduction.

II. Material And Methods

The present study is a retrospective study done at KIMS hospital. In this study 46 patients in the age group of 20-40 years were selected from the fertility centre and department of laboratory sciences of KIMS Hospital. The blood samples were collected from patients presenting to the sample collection, Department of Laboratory services, KIMS Hospital using Gel vacutainers (yellow) of BD type. 4ml of venous blood was collected between 3^{rd}-5^{th} day of the menstrual cycle after seperation of serum by centrifugation the sample measurements for AMH and FSH were measured.

AMH was measured by enzyme immunoassay method. Reading was taken on an ELISA reader and concentration of AMH was determined from the calibration curve by interpolation and values were reported in pM. FSH was estimated using electrochemiluminiscence immuno assay on cobes e411 fully automated analyzer, which automatically calculates the analyte concentration in mIU/ml using an instrument generated calibration curve. The result obtained was followed up with the Invitro fertilization (IVF) outcome and the patients were divided into 2 groups based on the outcome, group I in whom assisted reproduction did not help in conception or in whom there was premature loss of conception. Group II included patients in whom the IVF resulted in successful conception and favorable outcome with a live birth. The results of AMH and FSH were compared in these groups.

Inclusion Criteria: The selected patients included women with inability to conceive after 1 1/2 year of unprotected regular intercourse.

Exclusion Criteria : Those women in whom the male partner were found to be infertile and women with history of any cardiovascular disease, HIV, DM, TB, Asthma or any chronic diseases were excluded from the study. This study has been cleared by your Institution Ethics Review Board for human studies and that patients have signed an informed consent.

III. Results

Results of AMH and FSH obtained for group I and group II were analyzed using SPSS V-17.0 statistical software and it was observed that the mean AMH concentration was significantly higher in the group II (group that conceived) than group I . (P<0.002). It was also observed that AMH had a significantly positive correlation with the outcome and the (r) value was 0.529 at a 2 tailed significance of <0.001. When compared to FSH, it was observed that FSH had a significantly negative correlation to the outcome of pregnancy with r value -0.445. at 2 tailed significance of p<0.002. ROC curve analysis was done and it was observed that AMH was 83.3% sensitive and 77.3% specific at a best out off value of 18.5pM and FSH was 68.2% sensitive and 87.5% specific at a best cutoff of 10.15 mIU/ml, in assessing the outcome of IVF. It was also observed that AMH has a positive predictive value of 80.7% and negative predictive value of 88% on comparison FSH has a positive predictive value of 75% and negative predictive value of 83%.

Table: 1 Characteristics of study participants

	GROUP-I Mean ± SD	**GROUP-II** Mean ± SD	**t-value**	**p-value**
AMH	14.51±8.00	32.66±19.11	4.132	<0.001
FSH	12.07±5.42	7.70±3.40	3.298	<0.002

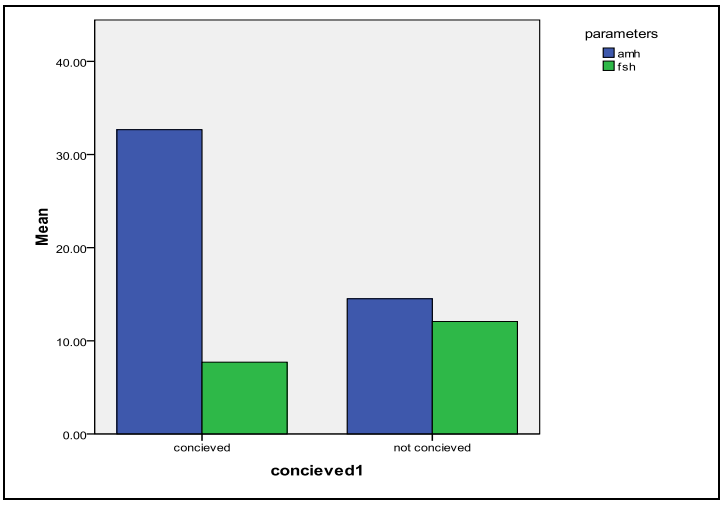

Table: 2 Sensitivity, Specificity and Cutoff points of AMH and FSH

	Sensitivity	Specificity	Best Cutoff value
AMH	83.3%	77.3%	18.5 pM
FSH	68.2%	87.5%	10.15µIU/ml

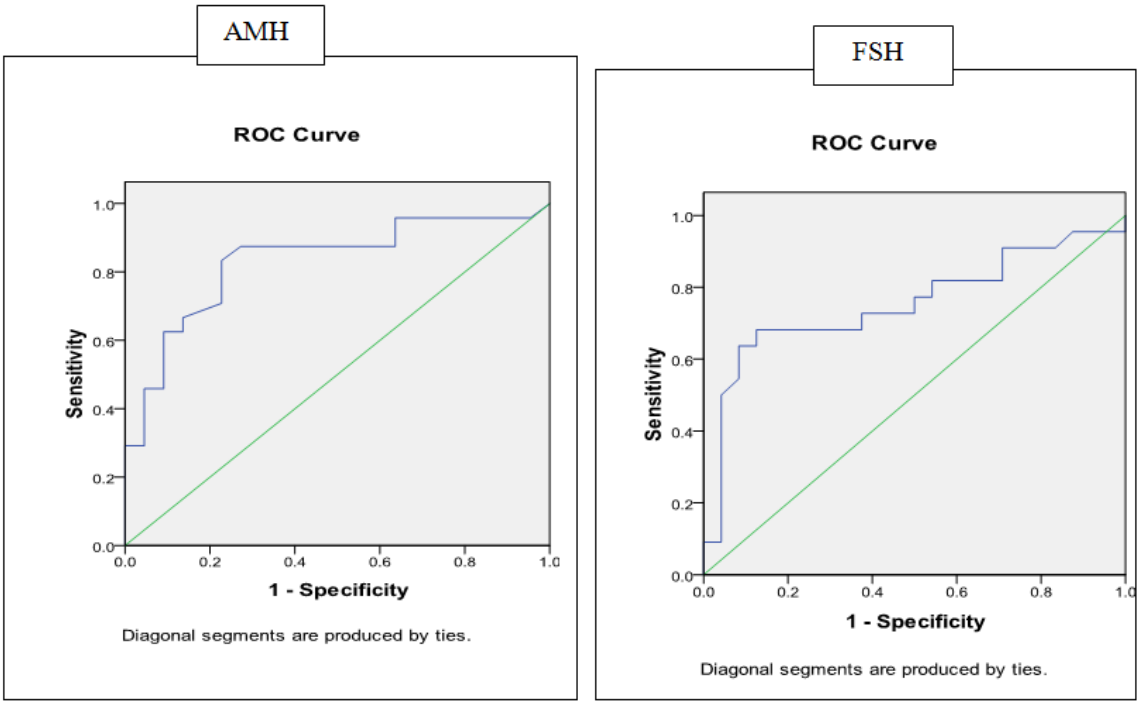

Table: 3 Correlation between studied markers and IVF outcome

	Correlation Value (r)	Significance
AMH	0.529	<0.001
FSH	-0.445	<0.002

Table:4 Predictive values of AMH&FSH in relation to IVF outcome.

	Positive predictive value	Negative predictive value
AMH	80.7%	88.0%
FSH	75.0%	83.0%

IV. Discussion

FSH belongs to the gonadotropin family; it is released in pulses from the gonad tropic cells of the anterior pituitary. In ovaries FSH stimulates the growth and maturation of follicle and hence also bio synthesis of estrogens in follicles. The FSH levels shows a peak at mid cycle and the levels of the circulating hormone are controlled by steroid hormones in a negative feed back to the hypothalamus[4,5]. Advancement of female age has been associated with slow and steady compensatory elevation of basal FSH, which is consistent with diminished ovarian reserve[8].

AMH a glycoprotein hormone in embryonic stage is secreted by sertoli cells of testes and is responsible for regression of mullerian ducts. Thus absence of AMH during embryogenesis allows the development of female sexual organs. After birth, AMH is produced in small amounts by ovarian granulosa cells. AMH levels in serum do not vary significantly either during menstrual cycle or between consecutive cycles.

It has been shown in the previous studies that AMH regulates the follicular recruitment by inhibiting the initiation of primordial follicle growth and preventing depletion of primordial follicle pool and there is increased sensitivity of follicular cells to FSH in absence of AMH[7]. Previous studies also showed that AMH levels decline over time as the available oocytes and surrounding granulosa cells decreases with age[7]. This suggested that there was a direct correlation between serum AMH and granulosa cell numbers. Thus AMH can be considered as a convenient and useful measure of assessing follicular reserve. Antral follicle count was previously demonstrated to be very useful in predicting the outcome but this procedure is technically challenging and user dependent, these features do not effect AMH testing and as AMH and FSH provide a view of the pool of primordial follicles. These tests thus measure the ovarian reserve and are useful tools for predicting the ovulation induction response.

In our study we observed that there is an inverse relationship between FSH and AMH with a significantly positive correlation between AMH and IVF outcome.

Using ROC analysis for prediction of outcome AMH had the best diagnostic accuracy with Area under the curve of (0.831) when compared to FSH (0.754).

Our study demonstrates that AMH at a concentration of 18.5 pM during reproductive age specifically differentiates between poor and good live birth chances. It suggests that women with higher AMH values tend to have better response to ovarian stimulation and have more eggs retrieved. We also observed that AMH has a high predictive value than FSH & both together are better negative predictors (i.e. in predicting absence of pregnancy success) for occurrence of live births. However there is no absolute value below which pregnancy cannot be achieved.

We thus conclude that AMH is a novel biomarker with multiple predictive capacities in IVF cycles, with low inter and intra cycle variation, which appears to be specific in assessing ovarian response to gonadotropins as long as the ovarian reserve is normal.FSH has pulsatile and circadian release in circulation, together with fluctuations in isoforms that may add to the potential errors. The predictive value of AMH is better than FSH, hence AMH can be considered as an ideal test to perform before the initiation of IVF cycle as it promises to address the aspects of human reproductive function and IVF.

V. Conclusion

The present study showed that there is a direct correlation between serum AMH and granulosa cell number. AMH levels decline over time as the available oocytes and surrounding granulosa cells decreases with age[7]. Thus AMH can be considered as a convenient and useful measure of assessing follicular reserve. AMH and FSH tests thus measure the ovarian reserve and are useful tools for predicting the ovulation induction response. There is an inverse relationship between FSH and AMH with a significantly positive correlation between AMH and IVF outcome.

Conflict of Intrests: The authors declare no conflict of intrest.

References

[1]. Clinical implications of ovarian reserve testing, volume 64, number 2, Obstetrical and gynecological survey, copyright © 2009, by Lippincott Williams and Wilkins.
[2]. The role of mullerian inhibiting substance in female reproduction, Curr opin obstet gynecol 20:257-264 © 2008 Wolters Kluwer Health/ Lippincott Williams and Wilkins 1040-872X.
[3]. Basal level of anti-Mullerian hormone is associated with oocyte quality in stimulated cycles.
[4]. Ebner T., Sommergruber M., Moser M., Shebl O., Schreier-Lechner E., Tews G.Human reprod., 2006, 21, 2022-6.
[5]. Assays for follicle stimulating hormone and luteinizing hormone: Guidelines for the provision of a clinical biochemistry service, Ann Clin Biochem 1987;24:246-262.Beastall GH, Ferguson KM, O'Reilly DSJ, Seth J, Sheridan B.
[6]. Relationship between ovarian steroids, gonadotropin and relaxin during the menstrual cycle. Acta Endocrinol 1983;129/2:121-125.Johnson MR, Carter G, Grint C, Lightman SL.
[7]. Anti-mullerian hormone as a marker of ovarian reserve.Obst.Gynecol.,2005,45,20-24 Tremellen K.P., Kolo M., Gilmore A., Lekamge D.N. Australian and New Zealand J.
[8]. Utility of serum antimullerian hormone/Mullerian- Inhibiting substance for predicting ovarian reserve in older women. Menopause: The journal of the North American Menopause Society, Vol. 15, No. 5, pp. 824-826, DO1: 10.1097/gme.0b013e31817c42f4, © 2008 by the North American Menopause Society.
[9]. Tests for ovarian reserve: reliability and utility.Curr Opin Obstet Gynecol 22:271-276.