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Research Article

SERUM ANTI MULLERIAN HORMONE LEVELS: A BETTER HORMONAL MARKER OF OVARIAN RESERVE

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ABSTRACT

Aim: To determine whether Serum AMH is a better hormonal marker of Ovarian Reserve. **Objectives:** 1. To correlate AMH with FSH and maternal Age and whether AMH is a better predictor of ovarian response than FSH. **Materials & Methods:** A total of 246 women enrolled for IVF-ICSI fulfilling the selection criteria were recruited for the study at a tertiary ART centre. On day 3 of the cycle serum AMH, FSH were assayed along with LH, E2, TSH and Prolactin. Within 3 months they were subjected to IVF-ICSI. Serum AMH and FSH levels were compared with Age and Oocytes retrieved. **Results:** All the 246 women enrolled were analysed. The mean age of the women was 30.7 ± 4.5 , average number of oocytes retrieved was 11.8 ± 7.1 . There was a negative correlation of AMH with age ($r = -0.28$) which is statistically significant where as FSH showed a positive correlation ($r = -0.27$). With regard to retrieval of mature oocytes, AMH showed a high positive correlation ($r = 0.60$) which is statistically significant ($p < 0.000$) when compared to serum FSH ($r = -0.26$). **Conclusion:** AMH is a better hormonal marker of Ovarian Reserve and a better predictor of Oocytes retrieved than serum FSH levels.

Key words: AMH, Ovarian reserve, ovarian response

INTRODUCTION

The success of IVF-ICSI depends on the number and quality of mature oocytes retrieved after controlled ovarian stimulation. Ovarian reserve is currently defined as the number and quality of follicles left in the ovary at any given time^{1,2} It is also defined as an estimate of oocytes remaining in the ovary that are capable of fertilization resulting in a healthy and successful pregnancy.³

In this era of advanced maternal age at the time of first child birth due to delaying child bearing have lead to increase in the incidence of infertility related to female reproductive ageing⁴

The conventional measure of assessing ovarian reserve by chronological age and FSH has several drawbacks. With age, there is a decline in ovarian reserve due to apoptotic loss of follicles and not due to ovulation⁵. So biological age of the ovary is not same as chronological age. FSH assay shows wide intra individual variability⁶. Clinically there is a need to identify women of relatively young age with reduced ovarian reserve as well as women whose fertility is naturally impaired by age who may still have satisfactory ovarian potential.

The present study is done to evaluate whether a) Serum AMH is a better hormonal marker of ovarian reserve than Serum FSH and Age. b) To determine

whether serum AMH is a better predictor of ovarian response than serum FSH levels.

MATERIALS AND METHODS

This was a prospective Observational study conducted at Infertility unit at a tertiary care centre from January 2011 to August 2013. A total of 246 women enrolled for IVF-ICSI were recruited for the study. Women in the age group of 20-45 years, with bilateral ovaries were included in the study and those women more than 45 years, hypogonadotropic hypogonadotropism were excluded. The informed consent was taken from all the participants and the Institutional Ethical committee approval was obtained. (IEC – NI/10/JUNE/17/17)

A detailed history and physical examination was done. On day 3 of cycle serum FSH, LH, Estradiol were assayed by the immune enzymometric assay ELISA technique. On the same day, serum sample for AMH assay was separated within one hour of venepuncture and was stored in aliquots at -40°C . The sample was later assayed in batches by AMH generation II assay, the analytical sensitivity was 0.14ng/ml and intra- assay and inter- assay CVs were <12.3 and < 14.2% respectively. These patients were subjected to Controlled Ovarian Stimulation within three months as per the unit protocol.

RESULTS

All 246 patients enrolled in the study were analysed. Among them, 72.8% were primary infertility; the female factor was the commonest indication for ICSI (32%) of which tubal factor accounted for 48%. This is followed by Male factor (24%), both (22%), Unexplained (14%), Donor (8%). The baseline characteristics are shown in table 1

Table 1: Baseline characteristics to include as table

Parameters	Values (n= 246)
Mean Age (years)	30.7 ± 4.5
Infertility duration (years)	7.2 ± 3.9
BMI (kg/m ²)	26.5 ± 4.7
FSH (mIU/ml)	7.2 ± 2.4
AMH (ng/ml)	4.5 ± 3.3
Mature Oocytes retrieved	11.7 ± 7.2

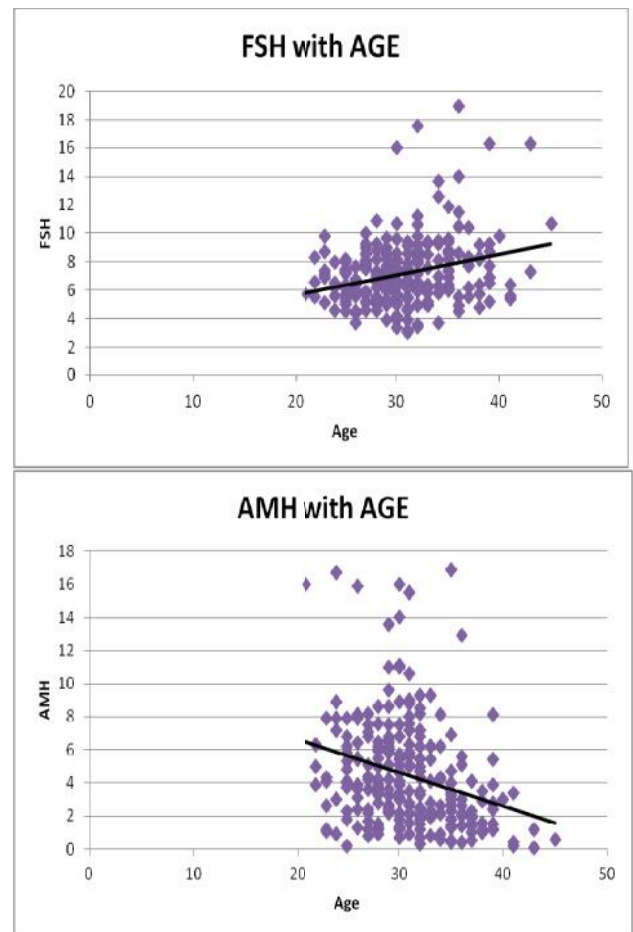


Fig 1 : Correlation of Age with AMH and FSH level

Correlation of Age with FSH showed a negative correlation ($r = -0.27$) where as with AMH (fig 1) showed a positive correlation ($r = 0.28$) which is significant ($p < 0.000$)

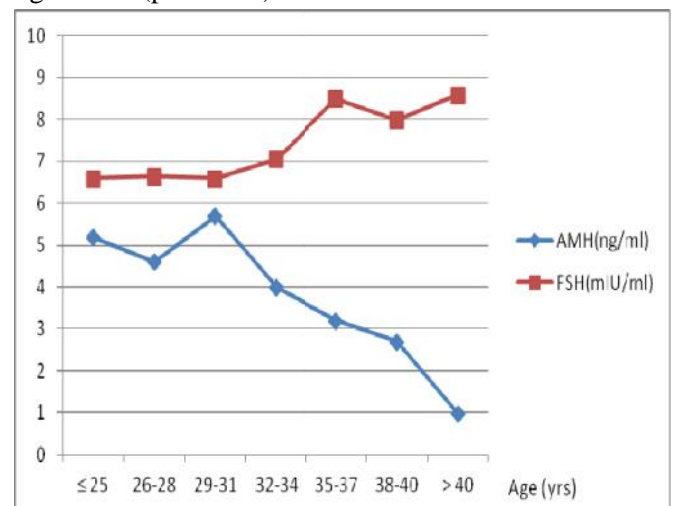


Fig 2 - the mean plasma levels of AMH and FSH according to age.

AMH levels show a decline after 30 years and FSH levels increase only after 35 years of age (fig 2).

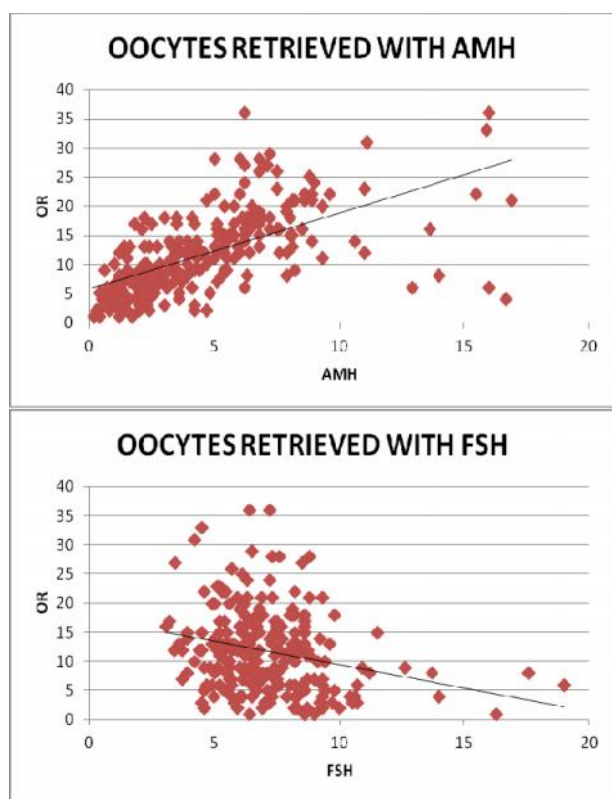


Fig - 3; Correlation of AMH and FSH with Oocytes retrieved

AMH showed a statistically strong positive correlation (fig 3) with the mature oocytes retrieved ($r=0.60$, p value 0.000) than FSH which showed a negative correlation ($r=-0.26$)

Statistical analysis: The collected data were analysed with SPSS 16.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis, means and standard deviation were used. To find significance difference in the multivariate analysis, the one way ANOVA with Tukey's Post - Hoc test was used. To assess the relationship between the variables Pearson's Correlation was used. To find the significance in categorical data Chi - Square test was used. In all the statistical tools, the probability value of $p<0.05$ is considered as significant level.

DISCUSSION

In this study the authors investigated the value of AMH as a marker of ovarian reserve in comparison with Age and FSH levels. As expected FSH levels rise and AMH levels decrease with increasing age. Interestingly, the sub group analysis of Age with AMH and FSH showed a static value with both till approximately 30 years of age at which point AMH levels showed a steady decline from 5.2ng/ml to 3.2

ng/ml by 37 years. Conversely the rate of change in FSH was discernable which started rising only after 35 years. This correlates with the study of de Vet et al, ⁷ a study of 41 women between 20 – 35 years showing a rapid decline in AMH levels with age. Another study of 238 patients with normal FSH values⁵ also showed a similar decline in AMH by 50% from 20-10pmol/L between 29 to 37 years of age and minimal changes in FSH values with age. This observation is very useful in this current trend of postponing the first child birth to the third decade for various social reasons. So early identification of diminished ovarian reserve by AMH assay in these individuals before it becomes critical will give the women a timely opportunity to advance the pregnancy plans, thereby maximising the chances of successful outcomes.

This study showed a statistically significant correlation between plasma AMH levels on day 3 of cycle and the ovarian response to controlled ovarian stimulation. This correlates with a pilot study done by Singh Neeta in the Indian population⁸ which showed a significant correlation between day 2 serum AMH levels and the oocytes retrieved in patients going for IVF. Our data strongly supports the previously published studies dealing with AMH levels and the marker of ovarian reserve and better hormonal predictor of ovarian response to controlled ovarian stimulation in Assisted Reproductive Technology ART cycles. It is an important, non invasive hormonal marker for early identification of diminished ovarian reserve than FSH levels. As this hormonal assay of AMH can be done any day of the cycle with less intercycle variability unlike FSH, it can be considered as an important tool for counselling the women who desire to post pone the first child birth, there by maximising the chances of successful outcome.

CONCLUSION

AMH is a better hormonal marker of Ovarian Reserve and a better predictor of Oocytes retrieved than serum FSH levels.

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