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Research Paper

To Study The Effect of Age And BMI on Markers of Ovarian Reserve in Indian Women with Primary Infertility of Age >35 Years

Medical Science

KEYWORDS : age, BMI, ovarian reserve, infertility.

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ABSTRACT

Objective:-To study the effect of age and BMI on transvaginal USG and hormonal markers of ovarian reserve and to correlate USG markers with hormonal markers.

Methodology: Fifty women with primary infertility of age >35 years having regular monthly cycles and no history of ovarian surgery were included in this cross-sectional study conducted from December 2010 until July 2011 in SMS Medical College. A transvaginal ultrasound to find out ovarian volume and antral follicles (AFC) and; blood tests for serum Follicle Stimulating Hormone (s.FSH) & serum. AntiMullerian Hormone (s.AMH) were carried out between the third and fifth day of their menstrual cycle.

Results: s.FSH increases with increasing age; and s.AMH, ovarian volume and antral follicle count decreases with increasing age (p value<0.05). No significant effect of BMI on s.FSH, s.AMH, ovarian volume and antral follicle count (p value > 0.05) was seen. There is highly significant negative correlation between s.FSH and ovarian volume & s.FSH and AFC.There is highly significant positive correlation between s.AMH and ovarian volume & s.AMH and AFC

Conclusion:-Age has significant effect on s.AMH, s.FSH, ovarian volume and antral follicle count while BMI does not significantly affect these markers. S.FSH increases with decreasing ovarian volume and antral follicle count while s.AMH decreases with decreasing ovarian volume and antral follicle count.

Introduction Ovarian reserve is an indication of reproductive age as opposed to chronological age and is a parameter of calculating remaining reproductive lifespan of woman. Diminished ovarian reserve is characterized by decreased number of remaining oocytes in the ovaries and impaired preantral oocytes development and recruitment. Over the past two decades, a number of tests of ovarian reserve have been used to determine follicle number and quality; and to predict the outcome of assisted reproduction procedures. The woman's age and assays of serum FSH in the early follicular phase were amongst the earliest and most useful parameters used for evaluation of ovarian reserve. Several ultrasound parameters have been used for evaluation of ovarian reserve, including ovarian volume, ovarian blood flow and the antral follicle count, with varying degrees of reliability. Recently, serum antimüllerian hormone levels have been introduced as a novel measure of ovarian reserve. AMH is a product of the granulosa cells in preantral and antral follicles. Serum AMH levels decline with age and are correlated with the number of antral follicles and the ovarian response to hyperstimulation.

The present study is intended to evaluate the effect of age and BMI on hormonal and USG markers of ovarian reserve and to correlate USG markers with hormonal markers.

Material and Method: This study was conducted in department of Obstetrics and Gynaecology, Sawai Man Singh Medical College, Jaipur between December 2010 to July 2011 on first 50 women coming for management of primary infertility who were >35 yrs. of age with regular menstrual cycles(excluding Male factor infertility, Tubal factor, Presence of gynaecological disorders such as menorrhagia or DUB, History of ovarian surgery & other causes of infertility).The study was approved by ethical committee and research review board of Sawai Man Singh Medical College, Jaipur.

Every case gave informed written consent prior to participation in the study. Cases were called on early follicular phase of menstrual cycle (day 1-3) and underwent transvaginal USG and Blood Tests. All Transvaginal USG was carried out by Toshiba Echo C using 7.5 MHz vaginal probe. The length, height and width of each ovary was measured in sagittal and coronal plane during TVS scanning and ovarian volume was obtained using formula of ellipsoid i.e., $\pi/6$ x (length x height x width).The number of antral follicles <10 mm in each ovary were counted.

Blood samples were taken for measurement of s.FSH and s.AMH .s.FSH was measured by standard MICT R FSH test kit-Magnetic Immunochromatic test-sensitivity 0.2mIU/ml and s.AMH was measured by ELISA (B.Lal laboratories diagnostic analytical sensitivity 0.2ng/ml)

Case's height (m) and weight (kg) were recorded and BMI calculated (kg/m2).The cases demographic information was recorded on predesigned schedule (religion/address/educational status/social status/medical &personal history).Other causes of primary infertility were excluded by obtaining history, doing clinical examination and standard diagnostic tests.

Results.

Women >35 years with primary infertility were included in the study according to age group they are divided into 3 groups i.e., 35-38 years,39-42 years & ≥43 years and then mean s.FSH, s.AMH, ovarian volume and antral follicle count taken out for particular age group and then standard deviation calculated and then level of significance calculated by ANOVA test. Significant effect of age was found over s.FSH, s.AMH, ovarian volume and antral follicle count. Thus s.FSH increases with increasing age; and s.AMH, ovarian volume and antral follicle count decreases with increasing age (p value<0.05) as shown in Table 1 below.

Cases were divided according to BMI into 2 groups as ≤25 and>25 and then mean & standard deviation of FSH, AMH, ovarian volume and antral follicle count calculated for particular BMI and then level of significance of effect of BMI on these markers. This study shows no significant effect of BMI on s.FSH, s.AMH, ovarian volume and antral follicle count (p value > 0.05) as shown in Table 1 below.

There is highly significant negative correlation between s.FSH and ovarian volume & s.FSH and AFC as shown in Table 2 below.

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There is highly significant positive correlation between s.AMH and ovarian volume & s.AMH and AFC as shown in Table 2 below.

TABLE-1

		S.FSH	S.AMH	OVARIAN VOLUME	AFC
AGE	PEARSON CORRELATION	.497	-.511	-.675	-.632
	SIG. (2-TAILED)	.000	.000	.000	.000
BMI	PEARSON CORRELATION	-.235	.047	.146	.088
	SIG. (2-TAILED)	.101	.747	.311	.546

CORRELATIONS BETWEEN MEASURES OF OVARIAN RESERVE&; AGE &BMI

TABLE-2

		OVARIAN VOLUME	AFC
S.FSH	PEARSON CORRELATION	-.489	-.364
	SIG. (2-TAILED)	.000	.009
S.AMH	PEARSON CORRELATION	.665	.644
	SIG. (2-TAILED)	.000	.000

CORRELATIONS BETWEEN MEASURES OF OVARIAN RESERVE AND S.FSH&S.AMH

Discussion: The present study observed highly significant effect of age on s.FSH, this is in accordance to the findings of G. Jurjen E. Oosterhuis et.al.1

It is revealed from the present study that there is no significant effect of BMI on s.FSH. This is similar to the findings of Samir Halawaty, MD, Eman ElKattan, MD et.al2.This is contrary to the results of **Helena Tinkanen, Merja Bläuer et.al3** who revealed from their study that FSH and BMI correlating negatively. This discrepancy may be due to difference in study design, racial difference and sample size

This study shows that there is highly significant effect of age on s.AMH, this is similar to the finding of de Vet A, Laven JS et.al4 & van Rooij IA, Broekmans FJ et.al 5which suggested that the mean ages at T(1) and T(2) were 39.6 and 43.6 years, respectively. The AMH and AFC were highly correlated with age both at T(1) and T(2), whereas FSH and inhibin B predominantly changed in women more than 40 years of age. These results indicate that serum AMH represents the best endocrine marker to assess the age-related decline of reproductive capacity.

This study shows no effect of BMI on s.AMH, this is similar to the findings of Samir Halawaty, MD, Eman ElKattan, MD 2et.al.This is contrary to finding of Erkan Buyuk, M.D,David B. Seifer, M.D et.al6 which suggests Elevated body mass index is associated with lower serum anti-mullerian hormone levels in infertile women with diminished ovarian reserve but not with normal ovarian reserve. This discrepancy may be attributed to difference in sample size, criteria used in study, sampling technique and racial difference.

This study shows highly significant effect of age on ovarian volume, this is in accordance to findings of **Sanja Kupesic et.al7&** A Lass, J Skull et.al8.which suggested that there is highly significant negative correlation of ovarian volume and age.

This study shows no effect of BMI on ovarian volume,this is contrary to the findings of Samir Halawaty, MD, Eman ElKattan, MD 2et.al.who found out that ovarian volume was significantly lower in obese women (3.7 ± 0.8 mL) than in non-obese women (6.6 ± 0.4 mL) (P = 0.03).This is also contrary to findings of Zaidi S, Usmani A, Shokh IS, Alam SE.9which suggested Ovarian volume showed decrease with an increase in the BMI, indicating the possible decrease in fertility with an increase in a woman's weight, this difference may be attributed to difference in selection criteria, sample size and sampling technique.

The present study observed highly significant effect of age on AFC. This is similar to the finding of Gabrielle et.al. 10 Mitchell, Barbara et.al11 & **Benny Almog M.D., Fady Shehata M.B. et .al12** who found out that antral follicle count decline with age in a white population is best described as a gradual acceleration in decline with age. Therefore antral follicle count alone should not be used to determine aggressive treatment because of fear of rapid loss of follicles.

This study shows no effect of BMI on AFC, this is in accordance to results of LG Nardo, D Gould, CT Fitzgerald, et.al[13] &Samir Halawaty, MD, Eman ElKattan14 which revealed that obesity has no association with levels of serum FSH, AMH, blood glucose, or AFC indicating that obesity is unlikely to affect ovarian reserve in the perimenopausal age group.

This study shows highly negative correlation between s.FSH and ovarian volume , this is in accordance to study of shahrara et.al15. which showed ovarian volumes and FSH and ovarian volume are correlated inversely. This is contrary to findings of Nozzhat Mousavifar16 et.al which showed there was no correlation between s.FSH and ovarian volume. This difference may be attributed to study design, sample size and selection criteria.

This study shows highly significant negative correlation of s.FSH and antral follicular count, this finding is similar to Pedro N. Barri Soldevila et.al17 & Peter.Y.K .Yong18 which suggested that there is significant correlation between s.FSH and AFC. Basal FSH was the most significant contributor to the number of oocytes, with a significant contribution from luteal phase AFC.

This study shows highly significant positive correlation of AMH and ovarian volume& AFC, this is similar to the finding of Yang YS, Hur MH et.al 19,Mei-Jou Chene et.al.20 & Joops. E. Laven et.al.21which shows serum AMH levels were more strongly correlated with AFCs than were serum levels of FSH, luteinizing hormone, and estradiol.

Conclusion

Age has significant effect on s.AMH, s.FSH, ovarian volume and antral follicle count while BMI does not significantly affect these markers.s.FSH increases with decreasing ovarian volume and antral follicle count while s.AMH decreases with decreasing ovarian volume and antral follicle count

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