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Factors Affecting Antral Follicle Count In Indian Women With Primary Infertility: A Descriptive Study.

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Abstract: *The objective of the study was to find out factors affecting antral follicular count in Indian women presenting for evaluation and management of infertility. This study was performed in Mahila Chikitsalaya, SMS Medical College, Jaipur from December 2010 to July 2011.A total of 50 cases were studied over this period. On the second to fourth day of the menstrual period, women with primary infertility having regular monthly cycles and no history of ovarian surgery underwent a transvaginal scan with colour doppler to determine ovarian volume, total antral follicle count (AFC) and ovarian stromal blood flow, and their serum FSH and AMH levels were checked.Ovarian volume alone(model-1) and ovarian volume along with ovarian blood flow(model-2) were found as predictor of antral follicle count .Both the model -1 and model-2 showed high significance in ANOVA table.(p value< 0.0001).Using model 1 and model 2 antral follicle count was predicted for each patient and their centiles (3^{rd}, 5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th}, 95^{th}& 97^{th}) were calculated .These centiles when plotted with their corresponding centiles of observed values of antral follicle count showed excellent agreement.*

Keywords: *antral follicular count, ovarian reserve, ovarian volume, ovarian blood flow, s.FSH, s.AMH.*

I. 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 [1]. It mainly depends on the number and quality of eggs in the ovaries and response of ovarian follicles to hormonal signals from the brain. 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 [2].The woman's age and assays of serum FSH in the early follicular phase were among the earliest and most useful parameters used for evaluation of ovarian reserve [3,4].

Several ultrasound parameters have been used for evaluation of ovarian reserve, including ovarian volume[5,6], ovarian blood flow and the antral follicle count, with varying degrees of reliability [7,8].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 [9]. Serum AMH levels decline with age and are correlated with the number of antral follicles and the ovarian response to hyperstimulation [10, 11].

A low AFC is a major factor in the diagnosis of poor ovarian reserve, that is, low fertility characterized by low numbers of remaining oocytes in the ovaries, usually accompanied by high follicle_stimulating hormone (FSH) levels. Several studies show that an AFC test is more accurate than basal FSH testing for older women (< 44 years of age) in predicting IVF outcome [12]. After the initial reports by Reuss etal. [13] and Scheffer et al. [14] that transvaginal ultrasonography could detect age-related decreases in follicle counts. Tomas et al. [15] and Chang et al. [16] introduced the antral follicle count (AFC) as an easy-to-perform and noninvasive method to provide essential information on ovarian responsiveness before initiation of gonadotropin stimulation in assisted reproductive technique. A low number of small antral follicles is associated with decreased ovarian response during controlled ovarian hyperstimulation for IVF, supporting the concept of reduced numbers of primordial follicles delivering a small antral follicle cohort. Moreover, Chang et. al.[17] reported a trend toward lower pregnancy rates in women with few antral follicles. Therefore the present study is an attempt to find out best predictor model to assess antral follicle count.

II. Materials And Methods

Indian women >35 years attending the department of Obstetrics and Gynaecology, Sawai Man Singh Medical College, Jaipur between December 2010 to July 2011 for management of primary infertility were

offered participation in descriptive observational study. The study was approved by Ethic Committee and Research Review Board of Sawai Man Singh Medical College, Jaipur.

Inclusion criteria for study were:

a) Women of primary infertility of age >35 years.
b) Regular cycles of 25-35 day with maximum 4 day difference between 2 cycles.
c) Presence of both the ovaries.

Exclusion criteria for study were:

a) Male factor infertility.
b) Tubal factor infertility.
c) Presence of gynaecological disorders such as menorrhagia or DUB.
d) History of ovarian surgery.
e) Other causes of infertility

III. Methodology

A detailed history and informed written consent was taken from every case 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 were carried out by same radiologist and carried out by using 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. Ovarian blood flow was seen in both the ovaries by Doppler study and those with resistivity index >0.5 was taken as poor blood flow and those <0.5 were considered normal blood flow (Barber et al. (1988))[17].Cases with poor blood supply even in one ovary were considered to have poor blood flow.

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).

Height(m) and weight(kg)were recorded and BMI calculated (kg/m^2).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.

IV. Results

All the data obtained were entered in excel spread sheet. Regression analysis was done by online MEDCALC software 14.0.0 to find out predictors of antral follicle count. Method of entry of independent variables was stepwise. Age, BMI, S.FSH, S.AMH, ovarian volume and ovarian blood flow were taken as independent variables. For normal and poor ovarian blood flow, 1 and 0 point were assigned respectively.

Probability of enter in the model was decided as <0.05 and probability of removal was ≥ 0.1.Ovarian volume was found as predictor in model-1 (R^2=0.784) and ovarian volume along with ovarian blood flow were found predictors in model-2 (R^2=0.803).Both the model -1 and model-2 showed high significance in ANOVA table. (p value< 0.0001)

Regression equation by model 1:-

(1) AFC= -1.446+1.761 X Ovarian Volume

And by model 2 was:-

(2) AFC= -0.643+1.43 X Ovarian Volume+1.32 X Ovarian Blood Flow

Using model 1 and model 2 antral follicle count was predicted for each patient and their centiles (3^{rd}, 5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th}, 95^{th}& 97^{th}) were calculated .These centiles when plotted with their corresponding centiles of observed values of antral follicle count showed excellent agreement. as shown in fig.1.

Thus, ovarian volume and ovarian blood flow were concluded as predictors of antral follicle count.

Table-1

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.885[a]	.784	.780	1.41565
2	.896[b]	.803	.795	1.36526
a. Predictors: (Constant), Ovarian Volume				
b. Predictors: (Constant), Ovarian Volume, Ovarian Blood Flow				

Table-2

ANOVA[c]						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	349.325	1	349.325	174.309	.000[a]
	Residual	96.195	48	2.004		
	Total	445.520	49			
2	Regression	357.915	2	178.957	96.010	.000[b]
	Residual	87.605	47	1.864		
	Total	445.520	49			
a. Predictors: (Constant), ovarian volume						
b. Predictors: (Constant), ovarian volume, Ovarian Blood Flow						
c. Dependent Variable: Antral Follicle Count						

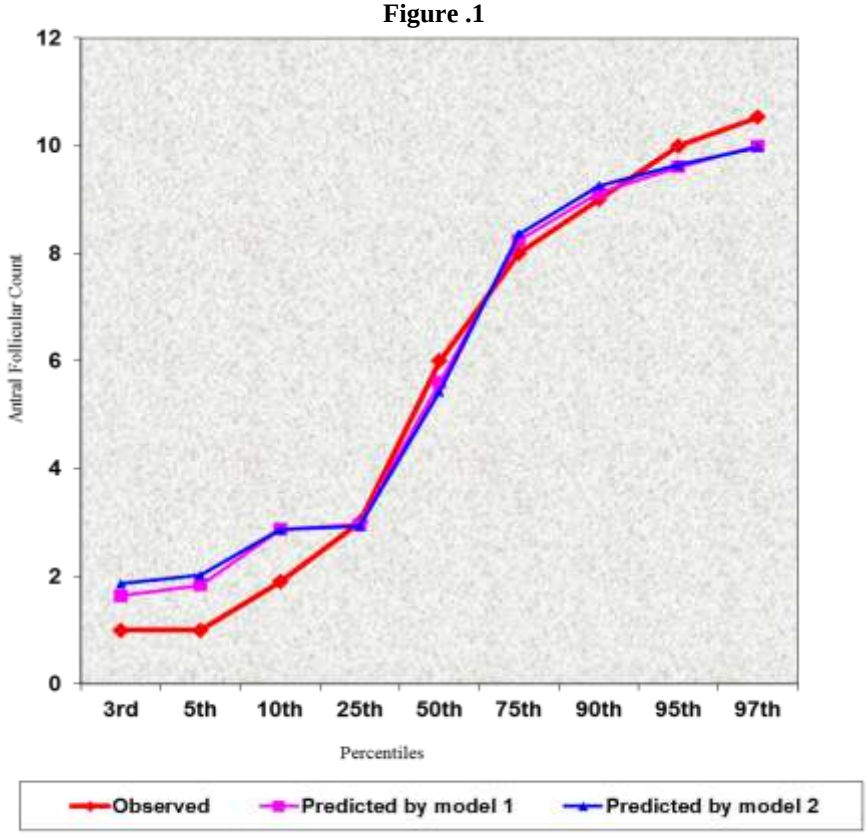
Table-3

Coefficients[a]						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-1.446	.573		-2.524	.015
	Ovarian Volume	1.761	.133	.885	13.203	.000
2	(Constant)	-.643	.667		-.965	.340
	Ovarian Volume	1.430	.201	.719	7.128	.000
	Ovarian Blood Flow	1.320	.615	.217	2.147	.037
a. Dependent Variable: Antral Follicle Count						

(1) AFC= -1.446+1.761 x ovarian volume

(2) AFC= -0.643+1.43 x ovarian volume+1.32 x Ovarian Blood Flow

Figure .1



Summary Statistics of Antral Follicular Count
(Observed & Predicted Values by different Linear Regression Models)

V. Discussion

The present study was conducted to find out the predictors of antral follicle count which showed that ovarian volume is significant predictor of antral follicle count. This is in accordance to the study of Erdem A, Erdem M et.al [18] which shows significant correlation between them($r = .777$, $P < .001$). It is also similar to the findings of John L Frattarelli et.al [19] which in their study showed that there is direct linear correlation was

observed between mean ovarian diameter and basal follicle number. It is again in accordance to the findings of J. Kline et.al. [20] which showed that Ln(1+antral follicle count) is most strongly related to Ln(1+follicle surface area) (r=0.76) and significantly associated with ovarian volume (r=0.48).

The present study found that ovarian blood flow as a predictor of antral follicle count which is similar to the findings of M A R Siddiqui et.al [21] which showed significant correlation between ovarian blood flow and antral follicular count.

VI. Conclusions

Antral follicle count is an important marker of ovarian reserve and a good predictor of the number of mature (dominant) follicles in a woman's ovaries that can be stimulated by medications leading up to IVF. Ovarian volume and ovarian blood flow are important predictors of antral follicle count in women with primary infertility.

Decreased ovarian volume and ovarian blood flow are associated with low antral follicle count. Knowing the ovarian volume and ovarian blood flow of women of particular age we can calculate the estimated antral follicle count and thus predict the ovarian response to stimulation.

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