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ULTRASOUND MEASUREMENT OF OVARIAN VOLUME AND ANTRAL FOLLICULAR COUNT IN NORMAL (FERTILITY PROVEN) AND INFERTILE WOMEN(THIRUVARUR)

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Abstract

Background: Infertility is a tragedy to the married woman and can be lead to marital upset, personal disturbances and poor health. Development in assisted reproductive technology has encouraged the use of newer techniques into routine practice reducing many investigatory procedures and the time delay. **Aim:** Our aim is to do the ultrasound measurement of ovarian volume and antral follicular count in normal (fertility proven) and infertile women (Thiruvarur). **Materials and Methods:** It is the Case-control study by using Transvaginal ultrasound. Transvaginal USG was carried out on the second or third day of the menstrual cycle. The basal ovarian volume and AFC were measured by endovaginal ultrasound. They were all compared to equal number of controls(fertility proven) in same age group(25-35yrs). **Results:** My observation indicates that the number of antral follicles is lower in sub-fertile patients than in fertile group (25 -35 yrs), in view of the significantly lower median AFC in women of the former group. The range of AFC in females presenting with complaints of infertility was 4-12(median value of 8). Inter-group comparison of median values of ovarian volume showed no significant difference in my study. This parameter however can be routinely measured without any added effort along with AFC. Though my data reflects that ovarian volume has no role as a bio marker of ovarian reserve **Conclusion:** The results of this study indicate that AFC is a viable predictor of fecundity in South Indian women of child bearing age in terms of capability to conceive on a two point scale (i.e. positive or negative).

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A cut off value of 8 may be used to prognosticate patients undergoing assessment for female factor infertility. Ovarian volume has no role as a biomarker of ovarian reserve
Keywords: transvaginal ultrasound, ovarian volume, antral follicular count.

Introduction

INFERTILITY

Infertility is the failure of a couple to conceive after 1 year of regular, unprotected intercourse. Ovulatory disorder is one of the most common reasons of female factor infertility 30% of all cases):

ETIOPATHOGENESIS

Categories Prevalence

Ovulatory factors 20 – 40 %
Male factors 20 – 30 %
Tubal factors 20 – 40 %
Endometriosis 4 – 6 %
Both male and female factor 10 – 40 %
Unexplained 10 – 20 %

OVARIAN CAUSES

FEMALE AGE AND DIMINISHED OVARIAN RESERVE

A strong association between increasing age of the infertile women and decreasing fertility rate has been documented well. In both spontaneous and ART cycles, Chronologic age of the mother is the strongest predictor of ovarian reserve and also the major determinant of reproductive success. However, increased maternal age per se has not traditionally been considered as a reason for infertility because it implies a physiologic condition than a pathologic condition. It has been found that fertility rates of women began to drop after the age of 30. After 1 year of inseminations procedure, the pregnancy rate in women aged 30 years and younger was 74% and decreased to 62% in women aged between 30 to 35 years, and considerably dropped to 54% in women more than 35 years of age.

OVARIAN RESERVE

The term denotes the capacity of the ovary to provide egg cells which is capable for fertilization results in a good outcome which in turn means a successful pregnancy. With advanced maternal age the capability of the ovary to produce egg cells will decline, constituting a major factor in the inverse correlation between age and female fertility The screening tests which are used in the estimation of ovarian reserve include estimation of serum FSH (follicle stimulating hormone) level on day 3, serum inhibin B level94, serum MIS level (mullerian– inhibiting substance63), CCCT (clomiphene citrate challenge test) and ultrasound parameters including ovarian antral follicle count and the mean ovarian volume measurement done transvaginally

ANTRAL FOLLICLE COUNT

Antral follicular count is referred as a number of oocytes and follicles in ovaries which is morphologically healthy and associated with serum concentrations of anti mullerian hormone. Anti mullerian hormone is a marker of quantity of healthy follicles and oocytes in ovaries. Antral follicular count measured by serial transvaginal ultrasonography during follicular phase is reproducible within an individual.

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OVARIAN VOLUME

Ovarian volume is an important tool in the screening, diagnosis and monitoring the treatment of conditions such as polycystic ovarian syndrome, ovarian cancer and adolescent abnormalities in reproductive medicine. Recent advances in technology, including the transvaginal scan have made possible the measurement of ovarian volume both easy and cost effective. Measurement of ovarian volume has a role in the assessment of ovarian reserve and prediction of response to superovulation

Materials And Methods

SETTINGS AND DESIGN

Case-control study

MATERIALS

Transvaginal ultrasound

***INCLUSION CRITERIA* CASES**

- Primary infertility
- No ovarian abnormality (polycystic ovary, ovarian endometriomas) as assessed by transvaginal USG.
- No evidence of uterine malformations or uterine pathology,
- no evidence of endocrinological disease
- no evidence of previous ovarian surgery

CONTROLS

- Proven natural fertility by having at least one pregnancy carried toterm
- Regular menstrual cycles,
- No evidence of endocrinological disease,
- No evidence of ovarian surgery,
- No ovarian abnormality as assessed by transvaginal USG, and

EXCLUSION CRITERIA

- any H/O ovarian abnormality like polycystic ovary, ovarianendometriomas
- History and any evidence of uterine malformations or uterinepathology,
- H/o endocrinological disease, and
- H/o previous ovarian surgery
- Hormonal contraception stopped > 3 months before entering thestudy protocol.

SAMPLE SIZE

Sample size for frequency in a population – 30 cases and 30 controls

SAMPLING METHODS

- All the patients attending gynecology outpatient department in reproductive age group (25-35yrs) who are all undergoing workupfor infertility are included
- They were all compared to equal number of controls(fertility proven) in same age group(25-35yrs).
- The basal ovarian volume and AFC were measured byendovaginal ultrasound.

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- Transvaginal USG was carried out on the second or third day ofthe menstrual cycle.
- Thorough survey of each ovary was done by scanning from theouter to the inner margin.
- All follicles having adequate morphology as described for a healthy follicle (i.e., 2-10 mm size range of well-defined anechoic cysts with smooth margins and absence of internal septations or nodularity) were measured and counted in each ovary. The sum of follicular count in both ovaries was labeled as Antral follicular count.
- The ovaries are measured in three planes and the ovarian volume was calculated using the prolate ellipsoid formula V=D1xD2xD3x0.523. D1, D2, D3 are the three maximal longitudinal antero-posterior and transverse diameters respectively.

Observation And Results

ROC CURVE FOR VARIABLES IN RELATION TO INFERTILITY

Comparison of ROC curves

Variable 1	Age
	Age
Variable 2	BMI
	BMI
Variable 3	OVARIAN
	VOLUME
	OVARIAN
	VOLUME
Variable 4	AFC
Classification variable	GROUP

Sample size		60
Positive group:	GROUP = 1	30
Negative group:	GROUP = 0	30

Group 1 –infertile group Group 0 – control group

	AUC	SE [a]	95% CI [b]
AFC	0.980	0.0105	0.905 to 0.999
OVARIAN_VOLUME	0.562	0.0757	0.428 to 0.690
BMI	0.557	0.0761	0.423 to 0.685
AGE	0.672	0.0697	0.539 to 0.788

AUC –area under the curveSE - Standard error

CI –confidence interval

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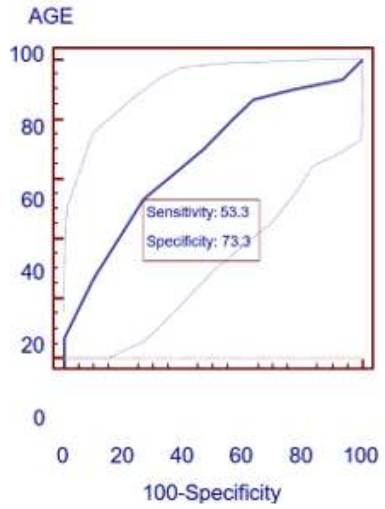
Variable 1

AGE DISTRIBUTION



Figure

AREA UNDER ROC curve - 0.67222 STATISTICAL SIGNIFICANCE P - 0.0134(<0.05)
Hence age is the significant variable to determine infertility with p value of 0.05

Variable	**AGE**
Classification variable	GROUP

Sample size		60
Positive group:	GROUP = 1	30
Negative group:	GROUP = 0	30

Area under the ROC curve (AUC)

Disease prevalence (%)	**Unknown**
Area under the ROC curve (AUC)	0.672222
Standard Error[a]	0.0697
95% Confidence interval[b]	0.538881 to 0.787914
z statistic	2.472
Significance level P (Area=0.5)	0.0134

[a] DeLong *et al.*, 1988

[b] Binomial exact

Youden index

Youden index J	0.2667
Associated criterion	>31

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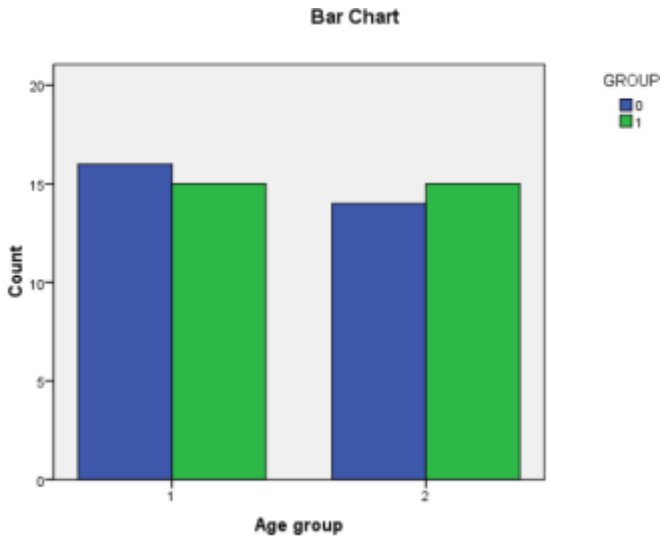

Figure

Age Group 1 –25–30yrs

Group 2 -31 -35 yrs

Among infertile group 15 in group 1, 15 in group 2

Among control group 16 in group 1, 14 in group 2

We also got the mean standard deviation of the both infertile and control group and found that there exists a statistical significance among the twogroups with response to age

Group statistics

group	**N**	**mean**	**Standard deviation**	**Standard error mean**	**Significance p**
Age 1(infertile)	30	31.30	2.466	0.450	0.019
0(control)	30	29.80	2.355	0.430	0.019

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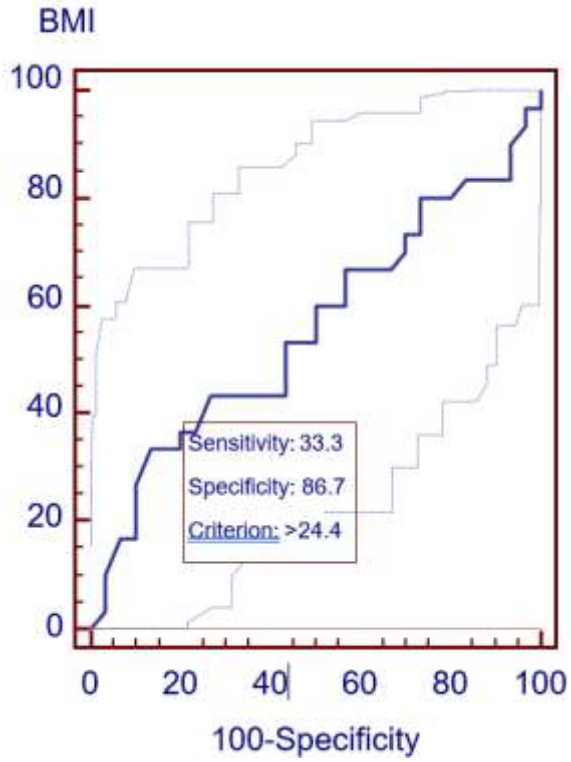
Variable 2
BMI



AREA UNDER ROC curve – 0.556667 SIGNIFICANT LEVEL P- 0.4568(>0.05)
Hence BMI is not a significant variable to determine infertility with significant level >0.05
BMI Group 1 –<25
Group 2 -≥25
Among infertile group 25 in group 1, 5 in group 2
Among control group 27 in group 1, 3 in group 2
We also got the mean standard deviation of the both infertile and control group and found that there is no statistical significance among the two groupswith response to BMI

Variable 3
OVARIAN VOLUME

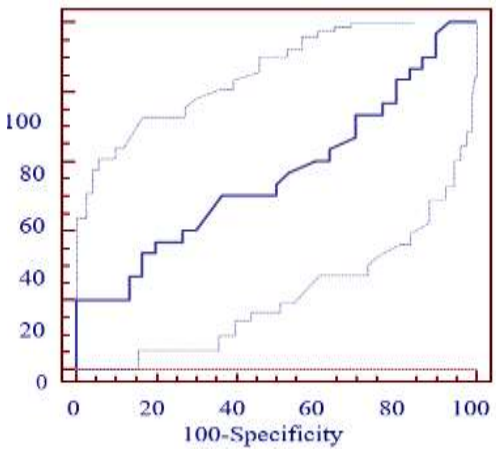


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Figure

Area under ROC curve – 0.562222 SIGNIFICANT LEVEL P – 0.4113(>0.05)

HENCE ovarian volume is not a significant variable to determine infertility

OVARIAN VOLUME Group 1 –9-11

Group 2 -≥11

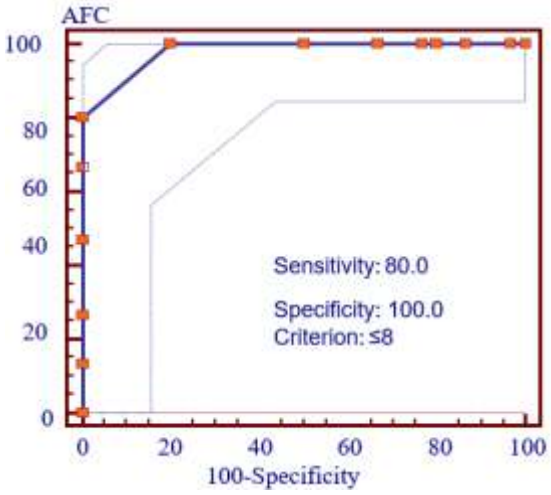
Among infertile group 15 in group 1,15 in group 2

Among control group 11 in group 1, 19 in group 2

We also got the mean standard deviation of the both infertile and control group and found that there is no statistical significance among the two groups with response to OVARIAN VOLUME

Variable 4

ANTRAL FOLLICULAR COUNT



Figure

Area under ROC curve – 0.980000Significant level p - <0.0001

Hence AFC is a significant variable to determine infertility with significant value of <0.05

AFI Group 0 –>8

Group 1-≤8

Among infertile group 6 in group 0, 24 in group 1

Among control group 30 in group 0, 0 in group 1

We also got the mean standard deviation of the both infertile and control group and found that there exists a statistical significance among the two groups with response to antral follicular count

Group statistics

group	**N**	**mean**	**Standard deviation**	**Standard error mean**	**Significance p**
AFC 1(infertile)	30	6.67	1.688	0.308	0.000
0(control)	30	11.23	2.112	0.386	0.000

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There existing a significant correlation between age and antral follicular count with significant level of 0.006

Discussion

Limited data is available on ovarian ageing in the sub-fertile and healthy population and the role of sonographic biomarkers (AFC, ovarian volume) of ovarian reserve. Most of the available data is based on studies outside India. The present study evaluates the relationship of AFC with age and BMI in sub-fertile cases and with healthy controls. Role of ovarian volume is also evaluated and compared with AFC.

My observation indicates that the number of antral follicles is lower in sub-fertile patients than in fertile group (25 -35 yrs), in view of the significantly lower median AFC in women of the former group ($P<0.001$). The range of AFC in females presenting with complaints of infertility was 4-12(median value of 8). The cut off value in Indian women is at a lower base line than that noted in the western literature. This variability in the value of AFC is most probably due to the differences in the ratio, socio- economic and geographic background of Indian and Western populations.

Though the reproductive ability of a woman is directly related to the remaining pool of primordial follicles at a particular point of time. This stock depletes as age progresses and is completely exhausted at menopause. Hence it may be reasonable to assume that the number of antral follicles reflects the ovarian pool and indirectly the reproductive age. My data shows that there is an inverse relation between AFC and the age of female (A negative correlation value $r= -0.4887$ with $p=0.0061$). The sensitivity of AFC to identify poor responders before induction of ovulation with exogenous gonadotrophins has been found to be around 89% in previous studies.

I however did not endeavor to establish any such correlation in our population as the same was out of scope of the study. I submit that the good correlation shown by my data between the afore mentioned parameters may be used in future by other Indian groups, evaluating metrics for patient selection during planning of ovulation induction. On evaluating antral follicles up to 10mm in diameter, significant difference in numbers was noted in my study population(6.67 ± 1.688 in cases; 11.23 ± 2.112 in controls; p value of <0.0001). A cut off value of 8 follicles (aggregrate of both ovaries) may be taken as a standard for successful pregnancy outcome.

Inter-group comparison of median values of ovarian volume showed no significant difference in my study. This parameter however can be routinely measured without any added effort along with AFC. Though my data reflects that ovarian volume has no role as a bio marker of ovarian reserve, I would like to suggest routine recording and further evaluation of role of this parameter in population based data sets.

Limitation

The major limitation of my study is its cross-sectional nature. Hence I could not conclusively establish the fact that lower AFC actually results in infertility. In addition while lower AFCs are seen among sub-fertile women at the time of presentation it could be ascertained from my data if this results from a smaller initial oocyte pool or an accelerated rate of loss.

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Longitudinal studies of AFC in both fertile and sub-fertile women will be necessary to determine the predictive value of AFC for future fertility.

Threshold values that predict a very low likelihood of spontaneous conception may be identified and thus the non-specific term "diminished ovarian reserve" currently overused in the infertility literature could gain clinical relevance among the general population. Pre ART (Artificial Reproductive Technique) ultrasonographic AFC has been shown to be an excellent predictor of ovarian reserve and response, with significant superiority in relation to other markers. Results from literature seem to converge for recognition of importance of AFC as a predictor of ovarian response.

Conclusion

- The results of this study indicate that AFC is a viable predictor of fecundity in South Indian women of child bearing age in terms of capability to conceive on a two point scale (i.e. positive or negative).
- The mean AFC in South Indian women is significantly different from that noted in Western literature, mainly due to racial, geographic and socio-economic reasons.
- A cut off value of 8 may be used to prognosticate patients undergoing assessment for female factor infertility.
- On the other hand same data can be utilized for optimum patient selection for ART. This would in turn lead to a higher success rate of this technique.

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