Original Article

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Ovarian Volume an Indicator of Ovarian Response following Ovulation Induction

Charulatha Baskaran*, Anthiyur Subramaniyam Allirathinam, Sundaram Senthil Priya***, Shankar Radhakrishnan******

Abstract

Background: Technological improvements in ultrasound machines and the use of high frequency vaginal probes allow investigators much closer access to the ovaries. The transvaginal ultrasound determinations of either the number of follicles of 2–5 mm diameter or the ovarian volume have been reported to define ovarian reserve and predict reproductive outcomes. Ovarian volume also predicts the occurrence of clinical pregnancy after IVF treatment. *Aim:* To assess ovarian volume as a predictor for ovarian response following ovulation induction and to correlate ovarian volume with FSH levels and other ultrasonographic parameters used to assess ovarian response. *Methodology:* A total of fifty infertile women with a history of primary or secondary infertility were included for study. The patients were asked to come on their 3rd day of menstruation, during which a thorough history, systemic examination and blood and radiological investigation were done. Ovulation was then induced using clomiphene citrate 50 mg/day from day 3 to day 7 of the cycle. To assess the post induction ovarian response patients were requested to come on day 12 for assessing the ovarian response through transvaginal ultrasound. *Results:* In the present study 60% of patients were within 30yrs of age. 58% of the patients had total ovarian volume <8.6cm^3. The total ovarian volume showed a negative correlation with the age. There was a positive correlation between number of follicles, size of follicles and total ovarian volume. Endometrial thickness had a weakly positive correlation with total ovarian volume. Basal FSH had no correlation with the ovarian response to ovulation induction. *Conclusion:* Ovarian volume can be determined before initiation of down-regulation and provides the clinician with a measurement of ovarian reserve that is determined readily, inexpensively, and with minimal invasiveness. Ovarian volume measurement should be an integral part of infertility evaluation.

Keywords: Total Ovarian Volume; Infertility; Ovarian Reserve; FSH.

*Post Graduate **Professor and HOD ***Associate Professor, Department of Obstetrics and Gynaecology ****Associate Professor, Department of Preventive Medicine, Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu 636308, India.

Corresponding Author:
Shankar Radhakrishnan,
Associate Professor,
Department of Preventive Medicine,
Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu 636308, India..
E-mail:
shnkr_radhakrishnan@yahoo.com

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Introduction

The human ovary is an organ which changes in size and activity throughout life. At birth, the ovary is ~1 cm in length and weighs <0.3 g. It has an elongated flattened shape that lies above the true pelvis.[1]The ovary is a composite of four embryological determinants: (i) germ cells, (ii) granulosa cells, (iii) germinal epithelium and (iv) mesenchymalstroma. They enlarge, increase in weight 30-fold, and change in shape, so by the time of puberty, they have reached the size, shape and weight of the adult ovary and lie within the true pelvis [2,3]. Adult ovaries are ovoid, measure approximately 3–5 cm by 1.5–3 cm by 0.6–1.5 cm and weigh 5–8 g. [1]. In early reproductive life they have a smooth white-pinkish exterior which later in life exhibits increasing numbers of retracted scars and convolutions. There are

by now three ill-defined zones in the ovary: an outer cortex, an inner medulla, and the hilus.

Technological improvements in ultrasound machines and the use of high frequency vaginal probes allow investigators much closer access to the ovaries. The result is high quality images with good resolution. Scanning of the ovaries is now a routine tool of every infertility clinic world-wide, to such an extent that operating in this field without ultrasound scanning is unthinkable. It is crucial in assessing the number and size of developing follicles in natural and stimulation cycles; the most important decisions when monitoring the cycle, such as adjusting the stimulation dose, timing the human chorionic gonadotrophin (HCG) injection and oocyte recovery, are taken according to the scan results. Estimation of ovarian volume and estimating its size are not common practice, nor is the relevance of ovarian size and its clinical implications in normal and pathological conditions clear [4].

Currently, there are very few publications on ovarian volume in normal healthy fertile (non-polycystic ovary (PCO)] women in their reproductive life [5,6]. Christensen *et al* measured the ovarian volume of 428 healthy women aged 14–45 who attended a family planning clinic [7]. They found that the ovarian volume was not correlated to age, height, weight and parity. While the smaller ovary remained the same volume throughout the cycle, the larger ovary increased in size from the beginning of the cycle to day 19 and decreased thereafter, due to the development of the preovulatory follicle in that ovary.

Ovarian reserve (OR) refers to the number and quality of oocytes that, at any given age, are available to produce a dominant follicle late in the follicular phase of the menstrual cycle. By estimating the OR, a prediction of the remaining reproductive lifetime could be assessed as well as the likely success of assisted reproductive techniques (ART) such as *in vitro* fertilization (IVF) [8]. The most commonly used biomarker test to assess ovarian reserve is the measurement of day 3 follicle stimulating hormone (FSH). Typically, Day-3 FSH and estradiol are both measured. However, other blood tests (antimüllerian hormone and, or inhibin-B) are gaining popularity since they provide more direct determination of ovarian status, whereas Day-3 FSH and estradiol are indirect measurements [9].

Thetransvaginal ultrasound determinations of either the number of follicles of 2–5 mm diameter or the ovarian volume have been reported to define ovarian reserve and predict reproductive outcomes [10,11]. Ovarian volume, separate from maternal age, predicts ovarian response to gonadotrophins as measured by the number of oocytes retrieved and cycle cancellation rates [12]. Ovarian volume also predicts the occurrence of clinical pregnancy after IVF treatment [13]. Most of the studies done so far are from western countries, in assessing ovarian volume as a predictor of ovarian reserve following ovulation induction, as of now only very few Indian studies had been done in this area. So, the current study will throw some light in accepting the ovarian volume as a marker for ovarian reserve, which is to be one of the cost effective investigation.

Aim

To assess ovarian volume as a predictor for ovarian response following ovulation induction and to correlate ovarian volume with FSH levels and other ultrasonographic parameters used to assess ovarian response.

Methodology

A prospective study was conducted during the period of Jan 2016 – December 2016 at our hospital in the out-patient department of obstetrics and gynaecology. Women in reproductive age group presenting with primary or secondary infertility were included in the study. Patients with history of partial or complete resection of ovary, ovarian cysts > 8mm in diameter and appearance of polycystic ovaries i.e. >10 follicles of < 9mm with hyperechogenicstroma were excluded from the study. A total of fifty infertile women who were fitting to our inclusion criteria were our study subjects. The patients were asked to come on their 3rd day of menstruation, during which a thorough history, systemic examination and blood and radiological investigation were done. Ovulation was then induced using clomiphene citrate 50 mg/ day from day 3 to day 7 of the cycle. To assess the post induction ovarian response patients were requested to come on day 12 and the following parameters were measured using the transvaginal ultrasound.

- Number of follicles – more than 3 follicles was considered significant
- Size of follicles – size of follicle > 18 mm was considered significant
- Endometrial thickness (m.m) – more than 8 mm was considered adequate response.

Ovarian volume was calculated using ellipsoid formula which is 0.523 x D1 x D2 x D3.

- D1 = maximum transverse diameter.
- D2 = maximum anteroposterior diameter.

- D3 = maximum longitudinal diameter.

Volume of smaller ovary and total ovarian volume that is sum of volumes of both ovaries were taken into consideration. Patients FSH levels were also assessed. All the data were entered and analysed using SPSS version 20. The socio-demographic data and preliminary analysis were done by simple proportions and percentages. The association between ovarian volume and other parameters were analysed using pearson's correlation.

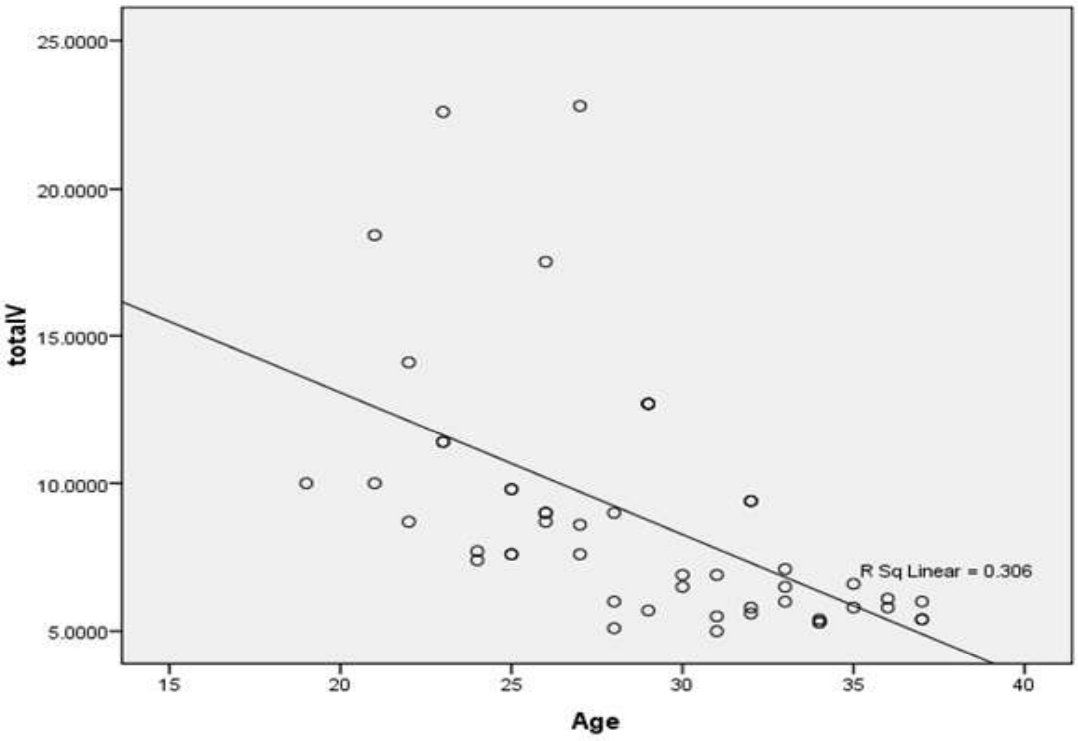
Results

The age wise distribution of the study subjects shows that majority (60%) of the infertile patients were in the age group of <30 years and only 10% of them were above 35 years with a mean age of 35.8 years (Table 1). The mean volume of the small ovary was 5.5 cm^3 and the mean total ovarian volume was 14.33 cm^3 which was measured after the ovulation induction by clomiphene citrate and the measurement was made on 12th day of the menstrual cycle. For majority (58%) of the study subjects the total ovarian volume was<8.6cm^3 and for another 38% of them the volume ranged between 8.6 – 22 cm^3 and only for 2% of the study subjects the total ovarian volume was more than 22 cm^3 (Table 2).

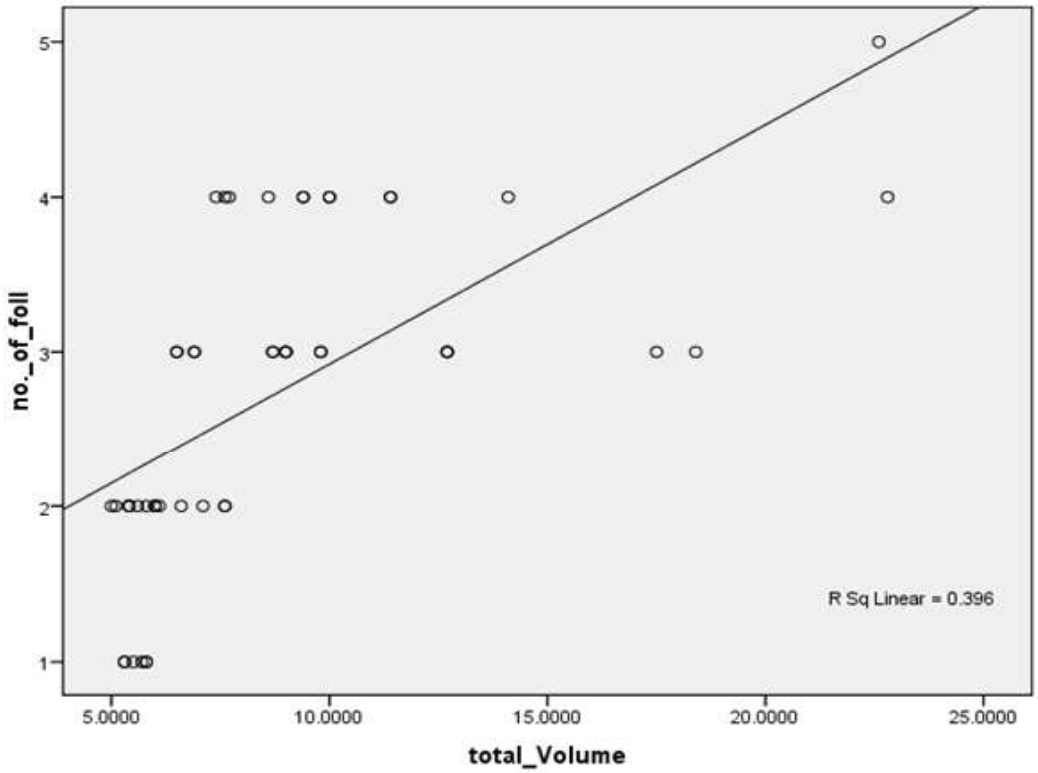
The correlations of ovarian volume with other parameters were studied. Maternal age found to have a perfect negative correlation with the total ovarian volume, as the age increases the total ovarian volume decreases (r = - 0.553) and this negative correlation found to be statistically significant (p<.05) (Graph 1). There is a positive correlation between total ovarian volume and number of follicles produced (the bigger the ovarian size the greater the number of follicles produced) with a coefficient correlation of 0.629, which is found to be statistically significant (P<0.05) (Graph 2).

Similarly there exist a positive correlation between total ovarian volume and size of follicles produced (the bigger the ovarian size the better the size of the follicle) with a coefficient correlation of 0.580, which is statistically significant (P<0.05) (Graph 3).

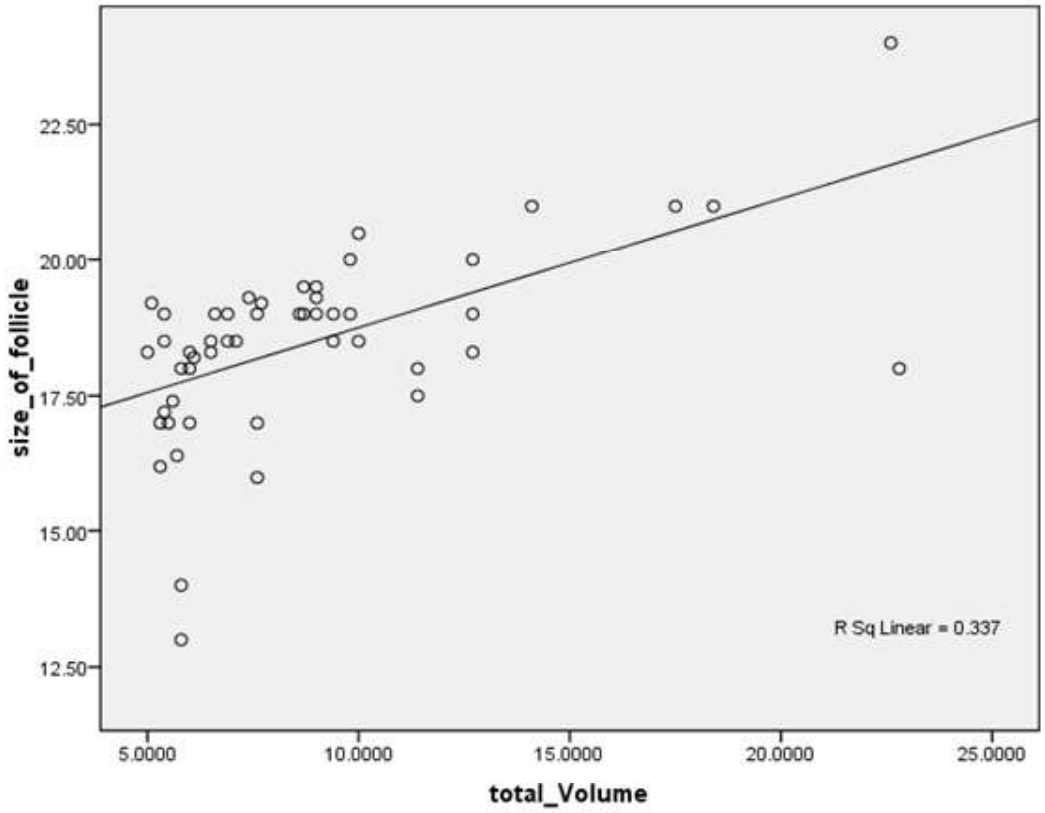
When seeing the association of total ovarian volume with endometrial thickness we found a weak positive correlation between total ovarian volume and endometrial thickness (the bigger the ovarian size the greater the increase in endometrial thickness) with a coefficient correlation of 0.351, which is statistically significant (P=0.012) (Graph 4).Whereas when correlated with FSH we found there was no correlation between total ovarian volume and FSH (r=0.001) (p = 1.00) (Graph 5).



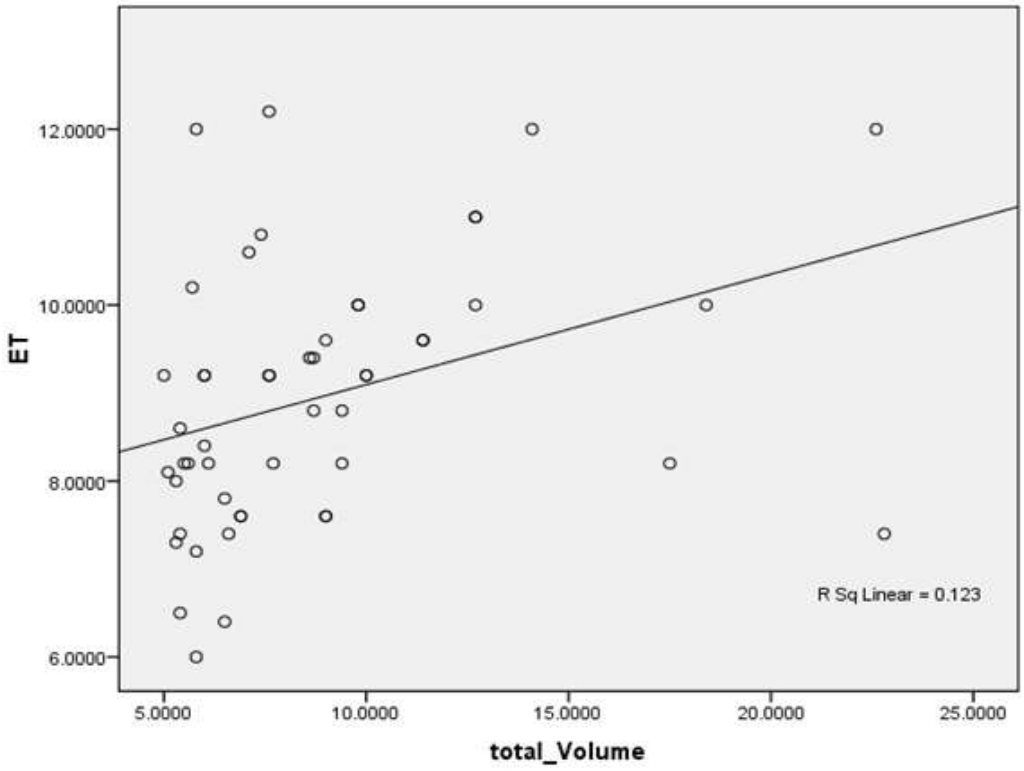
Graph 1: Correlation between total ovarian volume and maternal age



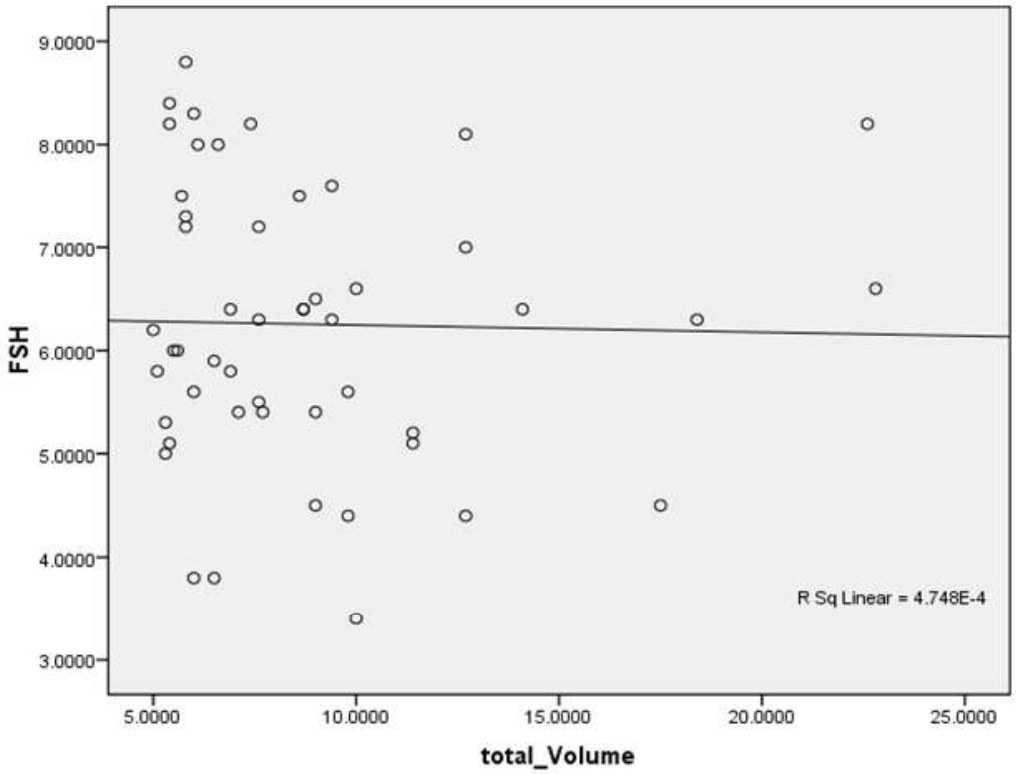
Graph 2: Correlation between total ovarian volume and number of ovarian follicles



Graph 3: Correlation between total ovarian volume and size of ovarian follicles



Graph 4: Correlation between total ovarian volume and endometrial thickness



Graph 5: Correlation between total ovarian volume and FSH

Table 1: Age wise distribution of the study population

Age group	Number(n)	Percentage (%)	Mean ± SD
<30	30	60	30.8 ± 4.5
31-35	15	30	
>35	5	10	
Total	50	100	

Table 2: Distribution of the study subjects according to the ovarian volume

Total volume of the ovary (cm^3)	Number(n)	Percentage(%)	Mean ± SD
<8.6	29	58	14.33±5.26
8.6-22.2	19	38	
>22.2	2	4	
Total	50	100	

Discussions

The present study had shown the age distribution of the patients varied between 18-37yrs, in which 60% of patients where within 30yrs of age and it is almost similar to the study done by Pai M.V etal [14] and another study done by NishaKanchan and Latha [15] where they had quoted that the maximum number of infertile women included in their study were < 30 years. In this study the 58% patient had total ovarian volume <8.6cm^3, 38% had 8.6-22.2cm^3, only 4% had total ovarian volume more than 22.2cm^3, and it is almost in par with the studies done by In the study by Pai MV et al [14]in which it is mentioned that 54% patients had TOV < 8.6 cm3 and 41% of patients had TOV between 8.6 and 22.2 cm^3 and a similar study done by NishaKanchan and Latha [15] had quoted that 62% of patients had total ovarian volume <8.6cm^3. 34% of patient had TOV between 8.6-22.2cm^3.

In the current study we found a statistically significant decrease in the total ovarian volume as the age of the women increases and this result was similar to the study done at Kentucky University where they screened 13,963 and they found a statistically significant decrease in ovarian volume with each decade of life from 30 to 70 years. Mean ovarian volume was 6.6 ml in women < 30 years, 6.1 in 30-39 years, 4.8 in 40-49 years. 2.6 in 50-59 years and 2.1 in 60-69 years [16] and in another study done by Aboulgha M etal [17], in which they have studied 512 patients who underwent oocyteretrieval for IVF and concluded that women's age had negative effect on IVF success and is more pronounced after the age of 36 years as ovarian volume decreases. The rate of follicle count starts declining from around 37 years, with approximately only 1000 follicles remains at the time of menopause. This substantiates the age related decrease in ovarian volume which is seen in the study.

In our study it was shown that when the ovarian volume is more the size of the follicles produced also bigger and similar type of results were also quoted by Syrop CH and Dawson JD in which they had mentioned that smaller ovarian volume showed retrieval of fewer mature oocytes implying less number of follicles developed in response to ovulation induction and less number of follicles had size > 18 mm [18].

In the current study a strong positive correlation was seen between the total ovarian volume and the number of follicles which means that both are directly proportional to each other and our findings were substantiated by other studies. In a study done by Lass A etal [19], the patients with ovaries < 3 cm^3 had 10.3 mean number of follicles and patients with ovarian volume > 3 cm^3 produced 14.5 mean number of follicles in response to induction of ovulation and in another study done by Frataerelli JL etal [20], mean ovarian volume < 2 cm^3 was associated with decreased number of follicles and mean ovarian volume of more than 2 cm^3 showed increased number of follicle and this relation using multiple linear regression analysis was found to be significant ($p < 0.001$) and a similar type of result was also shown by Sharara FY, Mc Clamrock HD et al [21].

Our study had highlighted that correlation between total ovarian volume and endometrial thickness is weakly positive, with endometrial response in terms of endometrial thickness > 8mm, it is contradicting to the study done by Pai MV et al [14] and by Nisha Kanchan & Latha [15], where they had shown that total ovarian volume and endometrial thickness had good correlation in terms of endometrial thickness >8mm

The present study had shown that there is no correlation between the day 3 basal FSH concentration and the total ovarian volume. In this

study the median FSH levels were 6.3mIU/ml with a mean of 6.25+/-1.3mIU/ml.Similarly a study by Craig H.Syrop etal,[18] showed that FSH value had a median of 8.5mIU/ml with a mean of 9.5+/- 4.0 mIU/ml. Linear regression showed no correlation between the ovarian volume to Day 3 FSH concentration. Hence they concluded that ovarian volume is a better measure of ovarian reserve than the FSH.

Conclusions

Ovarian volume can be determined before initiation of down-regulation and provides the clinician with a measurement of ovarian reserve that is determined readily, inexpensively, and with minimal invasiveness.Ovarian volume is a good predictor of ovarian reserve as it correlates well with post induction parameters like number of follicles in response to induction and endometrial response produced in response to induction. Ovarian volume measurement should be an integral part of infertility evaluation.

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