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Research Article

Assessing the Impact of Age on Ovarian Reserve: Insights from basal FSH and AFC Trends

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Abstract

This study aimed to evaluate the correlation between female age and ovarian reserve markers, specifically Day 2 follicle-stimulating hormone (FSH) and antral follicle count (AFC), and to determine the statistical significance of these relationships. We conducted a retrospective analysis of 371 women, aged 22 to 42 years, who were recruited for Assisted Reproductive Technology (ART) at a university-affiliated tertiary center between 2008 and 2013. Inclusion criteria required no history of ovarian surgery or hormonal therapy within the preceding three months, while exclusion criteria comprised a diagnosis of polycystic ovary syndrome (PCOS) or other endocrine disorders (e.g., thyroid dysfunction, hyperprolactinemia). Descriptive statistics summarized the data, and Pearson correlation coefficients were calculated to assess the relationships. A p-value < 0.05 was considered statistically significant. The analysis revealed a weak, non-significant positive correlation between age and Day 2 FSH ($r = 0.18$, $p = 0.446$) and a strong, significant negative correlation between age and AFC ($r = -0.61$, $p = 0.004$). These findings indicate that while Day 2 FSH is not significantly associated with age, AFC demonstrates a strong inverse relationship with advancing age, supporting its utility as a sensitive and reliable marker for ovarian reserve.

Keywords: follicle-stimulating hormone, antral follicle count, age, ovarian reserve, fertility

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1. Introduction

Ovarian reserve refers to the functional potential of the ovary, which encompasses the quantity of remaining oocytes. It is an essential factor in evaluating women who present with infertility or are planning assisted reproductive techniques (ART). As women age, ovarian reserve declines, which is associated with a decrease in both the number and quality of oocytes in the follicles [1, 2]. Although decreasing reserve is suggestive of reducing fertility, age is considered to be a better determinant of fertility when compared to ovarian reserve [3]. Recent studies have clearly mentioned that ovarian reserve does not predict fecundity [4]. Yet, understanding and evaluating ovarian reserve is fundamental for counselling patients regarding their reproductive prognosis and tailoring appropriate fertility treatment [5]. It should also be remembered that response and reserve are two different entities most of the times. Women with a high reserve may not respond to low-to-moderate doses of gonadotropins, whereas women with low reserve may respond well to even low doses of gonadotropins with all available follicles growing in an ART cycle.

Two key clinical markers used to assess ovarian reserve are basal (Day 2 or 3) Follicle Stimulating Hormone (FSH) and Antral Follicle Count (AFC). FSH is produced by the anterior pituitary and stimulates the growth of ovarian follicles. Elevated FSH levels early in the menstrual cycle are indicative of reduced ovarian feedback, suggesting a decline in ovarian function [5]. and probably a reduced response to exogenous gonadotropins in certain instances [6, 7]. It is also considered to have an antagonistic effect on granulosa cell viability [8]. Basal FSH measurement is cost-effective and widely available, making it a common tool in initial fertility assessments [5].

AFC, on the other hand, is determined by transvaginal ultrasonography and counts the number of antral follicles measuring 2–10 mm in both ovaries. It is considered a direct and reproducible marker of ovarian reserve and is closely associated with the pool of recruitable follicles [9]. Unlike FSH, which may fluctuate between cycles, AFC offers greater consistency and has demonstrated a stronger correlation with age and response to ovarian stimulation [3, 10].

The significance of accurately measuring ovarian reserve lies in its predictive value for response to controlled ovarian hyperstimulation (COH), probability of conception, and risk of ovarian hyperstimulation syndrome (OHSS). Thus, evaluating the strength of association between age, FSH, and AFC is vital in clinical practice.

This study aims to analyze the relationships among age, Day 2 FSH, and AFC using a well-defined cohort and to contextualize these findings with existing international data to enhance clinical relevance.

2. Materials and Methods

A retrospective analysis of case records was done using data from 371 women aged 22 to 42 years, who were recruited for Assisted Reproductive Technology in the Department of Reproductive Medicine &

Andrology (tertiary center affiliated to a university teaching hospital), Chettinad Super Specialty Hospital between 2008 and 2013. IHEC approval was not obtained as the data was obtained only from existing case records with the data being truly anonymized and de-identified.

Women who were recruited for ART procedure, with no history of ovarian surgery or hormonal therapy in the past three months were selected. And women who were diagnosed with polycystic ovary syndrome (PCOS) and endocrine disorders such as thyroid dysfunction and hyperprolactinemia were excluded. The data of age (in years), BMI (kg/m^2), Follicle Stimulating Hormone (FSH-IU/L) on day 2, measured using immunoassay techniques and Antral Follicle Count (AFC), counted by transvaginal ultrasound performed by a trained reproductive specialist were collected. Descriptive statistics were used to summarize the data. Pearson correlation coefficients were calculated between female age and each of the ovarian reserve markers. A p-value <0.05 was considered statistically significant.

3. Results

A total of 371 women were included in the analysis. The mean age was 30.9 ± 4.5 years. The mean BMI was 25.6 ± 3.7 kg/m^2. Mean Day 2 FSH was 7.43 ± 2.58 IU/L and mean AFC was 12.5 ± 5.9.

A weak positive correlation was seen between female age and Day 2 FSH (r = 0.18, p = 0.446), suggesting FSH rises slightly with age but not significantly. Whereas, there was a strong negative correlation between female age and AFC (r = –0.61, p = 0.004), indicating that antral follicle count significantly declines with advancing age (Figure **1**).

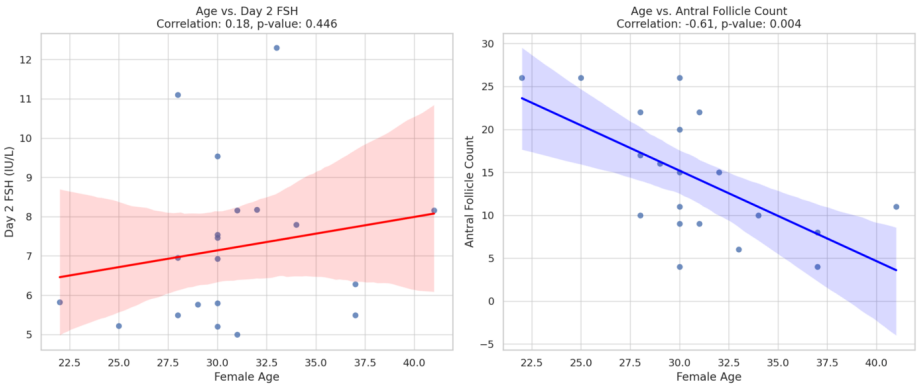

Figure 1: Scatter plot of Age vs. FSH (weak correlation, non-significant) and Age vs. AFC (strong correlation, significant).

The Pearson correlation coefficient between Day 2 FSH and AFC is –0.24, indicating a weak negative correlation—as FSH increases, AFC tends to decrease slightly. This suggests that: Higher Day 2 FSH levels are modestly associated with lower antral follicle counts. The relationship is not strong, but it aligns with the biological understanding that FSH tends to rise as ovarian reserve declines. Despite the weak strength of the correlation, the association is statistically significant (**p-value:** 0.000004) indicating that higher FSH levels are indeed associated with lower AFC values in this dataset.

After excluding women with polycystic ovaries, the mean AFC in different age groups is given as a graphical representation in Figure **2**.

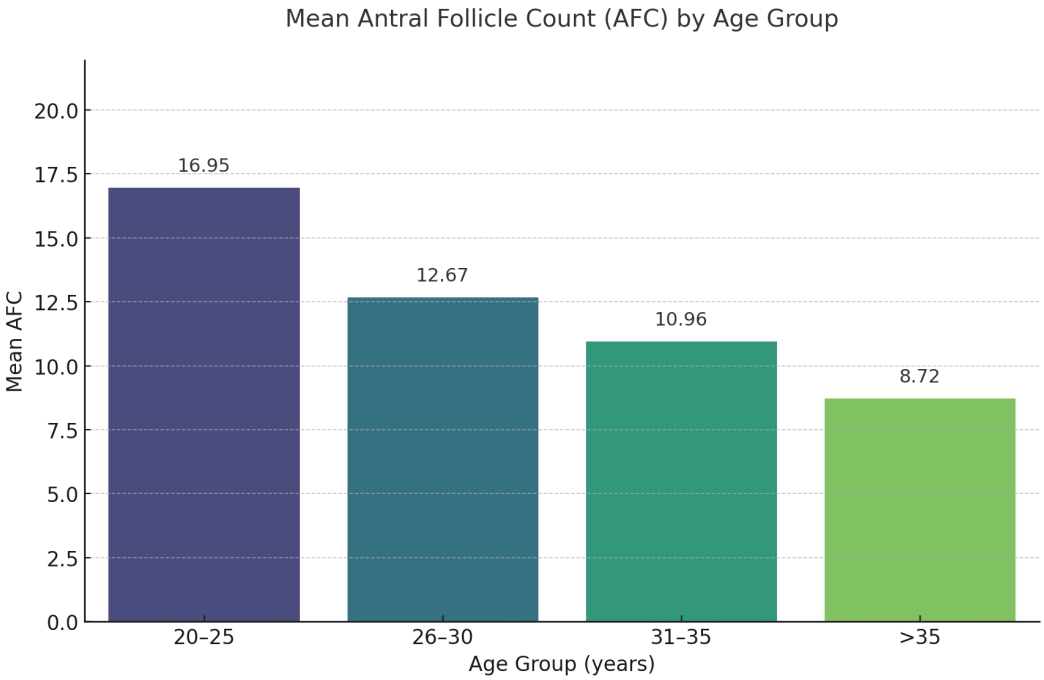

Figure 2: Mean AFC in different age groups.

4. Discussion

The study's findings align with the growing body of literature emphasizing the importance of AFC as a superior and reliable marker of ovarian reserve compared to basal FSH [10]. In our study, we do not expect an interobserver variability with the measurement of AFC, as all the scans were done by a single specialist.

AFC showed a statistically significant inverse correlation with age, reflecting the progressive decline in the follicular pool that accompanies female aging. This finding is consistent with large-scale studies, which have demonstrated similar patterns [11, 12].

In contrast, basal FSH levels displayed only a weak and non-significant correlation with age. This discrepancy may be due to the cyclical variation in FSH levels and its indirect reflection of ovarian activity. Several researchers have also highlighted that FSH levels can remain within normal limits until a critical threshold of follicular depletion is reached, at which point FSH levels rise dramatically [13].

A study comparing ovarian reserve in Caucasian and Indian women showed ovarian ageing of 6 years in advance in Indian women, suggesting significantly accelerated ovarian ageing in Indian women when compared to Caucasian women (Figure **3**) [14, 15].

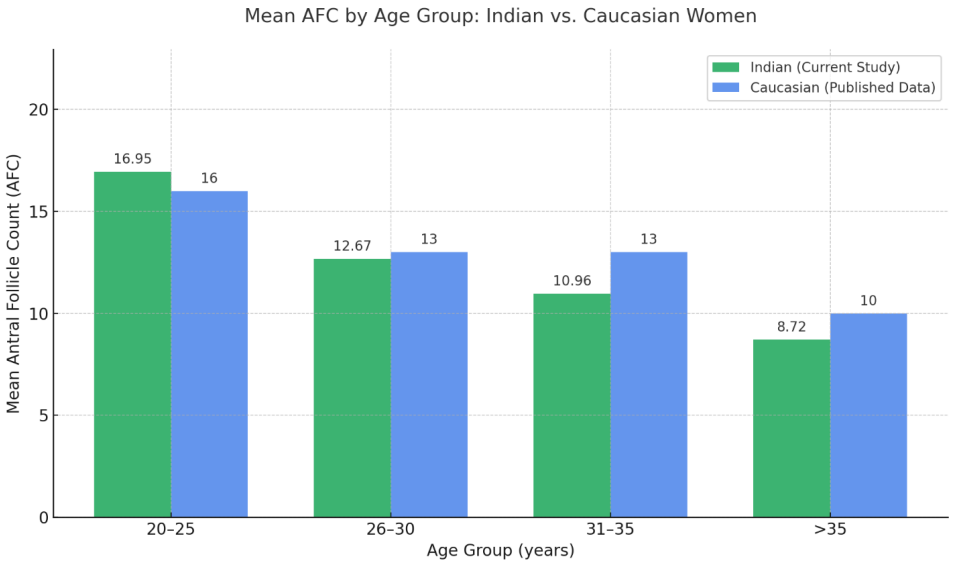

Figure 3: Comparison of mean AFC in the study group (Indian data) versus Caucasian women from published data.

Most other international data corroborate the findings of this study. For example, a Dutch cohort study reported mean AFC values of 16.2 at age 25, decreasing to 10.4 at age 35, and 6.2 at age 40. [16, 17] In contrast, the FSH levels in this cohort showed minimal elevation until age 37, after which a steep rise was observed. Similarly, a study from South Korea showed AFC values declining from a mean of 13.1 in women under 30 to 7.3 in women over 38, with a corresponding rise in FSH from 6.2 IU/L to 9.8 IU/L [18].

In comparison, the current study observed a mean AFC of 12.5 and FSH of 7.43 IU/L in an Indian population aged 22–42 years. These values are comparable to international data (Table **1**), suggesting a similar age-related decline pattern, although ethnic and lifestyle factors may introduce variability.

Table 1: Age-specific comparison of AFC in the study population and internationally published data.

Age Group (Years)	AFC (in numbers)	
	Study (Indian) Population	International Data
20–25	16.9	16.2
26–30	12.7	13.1
31–35	11.0	10.4
>35	8.7	6.2

An Indian multicenter study observed mean FSH levels of 6.8 IU/L (age: 25–29), increasing to 8.9 IU/L (age 35–39), with AFC declining from 14.2 to 7.5. (13) A classic study of Chinese women with proven fertility found that AFC declined at about 3.8% per year with increasing age [19]. No difference was ever observed in the ovarian reserve of fertile and infertile women, proving that ovarian reserve may not be a direct predictor of fertility. [20] European registry data from the Netherlands report a mean FSH of 6.5 IU/L in younger age groups and a median AFC of 12.8 (ages 25–30), decreasing to 6.1 (ages 38–42) [21].

The clinical implications of these findings are noteworthy. AFC, being a direct ultrasonographic measure of the follicular pool, provides more reliable guidance for clinicians when deciding fertility treatment

protocols. It is particularly useful in predicting ovarian response in controlled ovarian hyperstimulation and assessing the risk of poor or excessive response [22]. The consistency of AFC across menstrual cycles and its strong association with age make it a valuable tool for individualizing fertility care [10].

Limitations: Limited sample size and Retrospective design.

Future Directions: Longitudinal studies tracking changes within individuals over time could add depth to the cross-sectional findings.

5. Conclusion

Antral Follicle Count significantly declines with age and is more reliably correlated than Day 2 FSH or AMH. AFC should be emphasized in fertility evaluations, particularly in counselling women regarding the expected response or the risk of hyperstimulation. As per guidelines and results from our study, AFC would be the best indicator of ovarian reserve and thereby response when the ultrasound is carried out by a trained specialist. While counselling women for fertility treatment, it is also crucial to explain the ethnic variations observed in the ovarian reserve.

Declarations

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Nil

Conflicts of interest

Nil

Ethical Approval

IHEC approval was not obtained, as the data was obtained only from existing case records, with the data being truly anonymized and de-identified.

Data Availability Statement

The clinical data of this article are available upon reasonable request to the corresponding author.

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