Original Article

Prediction of Poor Ovarian Response during *In vitro* Fertilization in Nigerian Women: A Comparison of Basal Antral Follicle Count and Follicle-Stimulating Hormone

David Tolulope Ejenobo[1], Nkeiruka Ameh[2], Joseph A. M. Otubu[3], Bolarinde Ola[4], Ibrahim Wada[1], Augustine Monday Onuh[5]

[1]Department of Obstetrics and Gynaecology, Nisa Premier Hospital, [3]Centre for Reproductive Health Research, [5]Department of Obstetrics and Gynaecology, Garki Hospital, Abuja, [2]Department of Obstetrics and Gynaecology, Ahmadu Bello University, Zaria, Nigeria, [4]Department of Obstetrics and Gynaecology, Jessop Wing and Royal Hallamshire Hospitals, Sheffield Teaching Hospitals NHS Trust Foundation Trust UK, Sheffield, UK

Abstract

Background: Poor ovarian reserve has been shown to be associated with poor outcomes of *in-vitro* fertilization (IVF) treatment. Women who can be reliably identified as expected poor responders can be advised on chances of poor outcomes that may dissuade them from wasting resources on IVF using their own eggs; and offered donor eggs, especially in a resource-poor country like Nigeria. Many centres routinely perform basal follicle-stimulating hormone (FSH) assay before IVF; however, basal antral follicle count (AFC) has emerged as a more reliable test of ovarian reserve that can be provided at a reduced cost compared to FSH in an IVF clinic setting. The determined predictive values of basal AFC compared to FSH in Nigerian women can be used to predict poor ovarian response during IVF treatment; and also to influence local clinical practice in IVF by offering a more reliable and affordable test, thereby avoiding wastage due to duplicate and unnecessary investigations. **Aim:** The aim is to determine the diagnostic accuracy of basal AFC compared to basal FSH for the prediction of ovarian response during the IVF cycle in Nigerian women. **Patients, Materials and Methods:** This was a hospital-based prospective comparative study in two private fertility centres in Abuja. Consecutive 166 women that underwent IVF treatment cycles who met the inclusion criteria were recruited. On day 2 to day 4 of a normal cycle, FSH assay and AFC using the Broekmans' systematic process were done. They had controlled ovarian hyperstimulation by antagonist or agonist and occasionally long protocols. The poor response was defined as <4 follicles of >17 mm on the day of human chorionic gonadotropin trigger or ≤3 oocytes retrieved. Receiver operating characteristics (ROC) analysis was done to determine the level of the area under the curve (AUC) and optimum cut-off values of FSH and AFC in predicting poor ovarian response. **Results:** Twenty-eight (16.9%) had poor responses. ROC analysis demonstrated that AFC had the largest (AUC = 0.707, $P = 0.001$) relative to FSH (AUC = 0.591, $P = 0.128$). The ROC analysis showed that the optimum cut-off value for the prediction of poor response for AFC was ≤10, which had a higher accuracy of 67.5%, while for FSH was ≥8.15 mIU/ml with a lower accuracy of 61.5%. They both had the same sensitivity of 60.7%; however, AFC had better specificity, negative and positive predictive value, and higher odds ratio for the prediction of poor ovarian response. The positive and negative likelihood ratios of both cut-off values suggest that they may not be useful as diagnostic tests. **Conclusion:** ROC analysis estimated that AFC more accurately predicts poor ovarian response by its larger and more significant AUC compared to FSH in our population of women.

Keywords: Antral follicle count, follicle-stimulating hormone, *in-vitro* fertilization, ovarian reserve, ovarian response

Introduction

The decline in female fertility due to reproductive aging has led to an increased demand for assisted reproductive technology (ART) services to provide conception and eventual live birth.[1,2] The success of ART treatment cycles is unfortunately low when the ovarian reserve is poor. Poor ovarian reserve (POR) due to advancing reproductive age

Access this article online

Quick Response Code:

Website: www.njmonline.org

DOI: 10.4103/NJM.NJM_18_22

Address for correspondence: Dr. David Tolulope Ejenobo, Department of Obstetrics and Gynaecology, Nisa Premier Hospital, Plot 15–21 Alex Ekwueme Way, Jabi, (P. O. Box: 7320, Wuse) Abuja, Nigeria.
E-mail: davidejenobo@yahoo.com

How to cite this article: Ejenobo DT, Ameh N, Otubu JA, Ola B, Wada I, Onuh AM. Prediction of poor ovarian response during *in vitro* fertilization in Nigerian women: A comparison of basal antral follicle count and follicle-stimulating hormone. Niger J Med 2022;31:611-7.

Submitted: 29-Jan-2022 **Revised:** 04-Nov-2022
Accepted: 30-Nov-2022 **Published:** 28-Feb-2023

has been shown to be related to poor response to ovarian stimulation and negative outcome of ART.[3,4]

POR is associated with a decline in oocyte yield during *in-vitro* fertilization (IVF), reduced pregnancy, and live birth rates. Prediction of individual ovarian response to exogenous gonadotropin is one of the most important strategies for successful and safe IVF treatment.[4,5]

No single parameter has so far been shown to give satisfactory prediction of ovarian reserve or pregnancy following an IVF cycle.[6] However, the ovarian antral follicle count (AFC) has emerged as a useful predictor of ovarian response and stimulation quality in ART within an IVF clinic setting. Ovarian antral follicles larger than 2 mm are extremely sensitive and responsive to follicle-stimulating hormone (FSH) and are defined as "recruitable."[7] They can be visualized and measured with transvaginal ultrasound, and the total number of 2–10 mm follicles in both ovaries represent AFC and are expected to be at least 5–7 in normal ovarian reserve.[8] Hence, AFC estimates with very good accuracy the extent of the pool of follicles on which the exogenous FSH will act. It has also been shown that in the prediction of chronological age in normal women, the number of antral follicles appears superior to other presumed measures of reproductive aging.[9]

AFC has been shown to be the most significant parameter for the prediction of the number of embryos achieved with ART which has made it a useful tool in advising patients and individualizing the dose of exogenous gonadotrophins used during ovarian stimulation.[7]

In an IVF clinic setting, basal AFC does not have additional costs to patients. It is easy to determine, has low inter-cycle variability and has low to moderate inter-observer variability.

Very few studies have looked at the predictive value of AFC in Nigerian women. This study provides knowledge of the predictive values of basal AFC in Nigerian women and how it compares with basal FSH.

The objectives of the study were to determine the diagnostic accuracy of basal AFC in predicting ovarian response in Nigerian women using receiver operating characteristic (ROC) curve, to determine the diagnostic accuracy of basal FSH in predicting ovarian response in Nigerian women using ROC curve, to compare the diagnostic accuracy of AFC and FSH for poor ovarian response and cancelled IVF cycles in Nigerian women by comparing their area under the curve (AUC), to determine the cut-off value of basal AFC and FSH that gives best sensitivity and specificity for poor ovarian response in Nigerian women and using the diagnostic cut-offs, to determine the likelihood ratios (LRs) of a positive and negative test for expected poor ovarian response using the basal AFC and FSH cut-offs determined.

Patients, Materials and Methods

This was a hospital-based prospective comparative study carried out in Garki and Nisa hospitals based in the FCT Abuja, Nigeria. The Garki and Nisa hospitals are a public–private partnership that facilities receive clients for IVF from different parts of the country; however, majority of the clients are residents of Abuja. Both facilities combined carry out 900 IVF cycles per year. The study population comprised clients who are undergoing IVF using their own eggs who consented to the study, having both ovaries present, with no current or past diseases or surgeries affecting the ovaries, who have not had chemotherapy or pelvic radiotherapy in the past, not on any form of hormone therapy, no history of autoimmune disease, and both ovaries are adequately visualized at transvaginal ultrasound scanning. Patients were excluded from the study if they had polycystic ovary disease, endometriotic ovarian cysts, dermoid ovarian cysts, other cystic masses of the

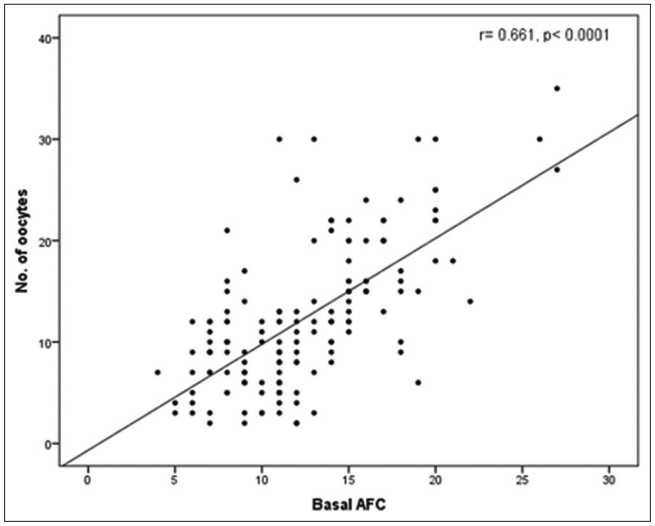

Figure 1: Correlation between basal AFC and number of oocytes retrieved. AFC: Antral follicle count

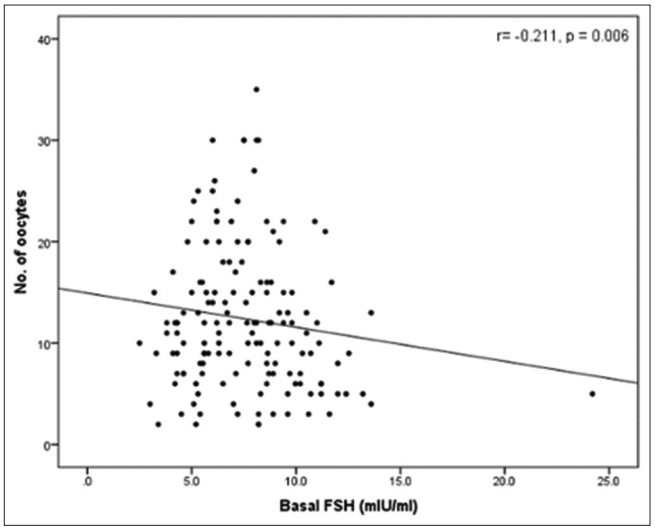

Figure 2: Correlation between basal FSH and number of oocytes retrieved. FSH: Follicle stimulating hormone

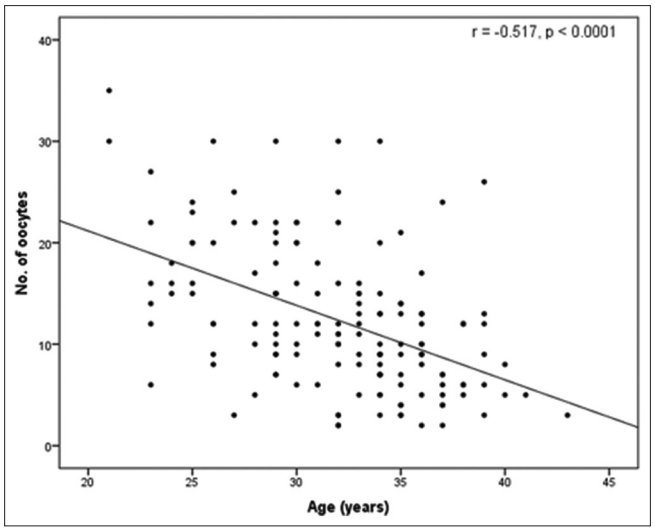

Figure 3: Correlation between age and number of oocytes retrieved

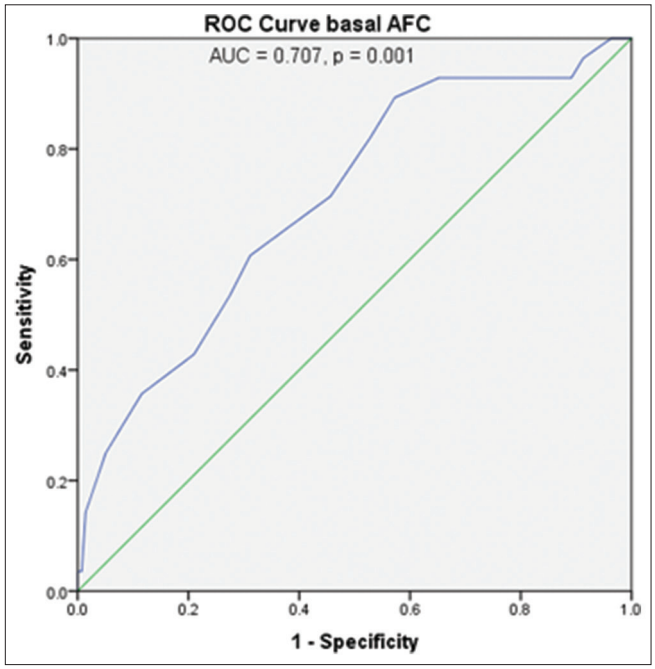

Figure 5: Basal AFC ROC curve for poor ovarian response. AFC: Antral follicle count, ROC: Receiver operating characteristics

ovary >2 cm, or solid ovarian mass of any size. Patients that had Embryo recipient cycle, on medication that could interfere with the hypothalamic–pituitary–gonadal axis in the preceding 3 months to the study or withhold consent for the study were also excluded.

This study was reviewed by the Research and Ethical Committees of the Federal Capital Territory Administration, and permission was obtained from the committee to carry out the study. The sample size required was calculated with the sample size formula for surveillance or detection of disease (diagnostic investigations).[10,11]

The sample size was calculated with the following formula

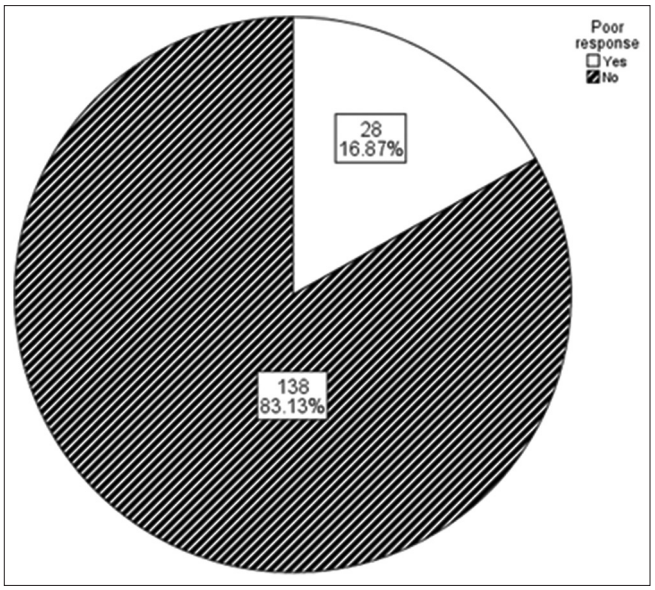

Figure 4: Frequency of poor responders

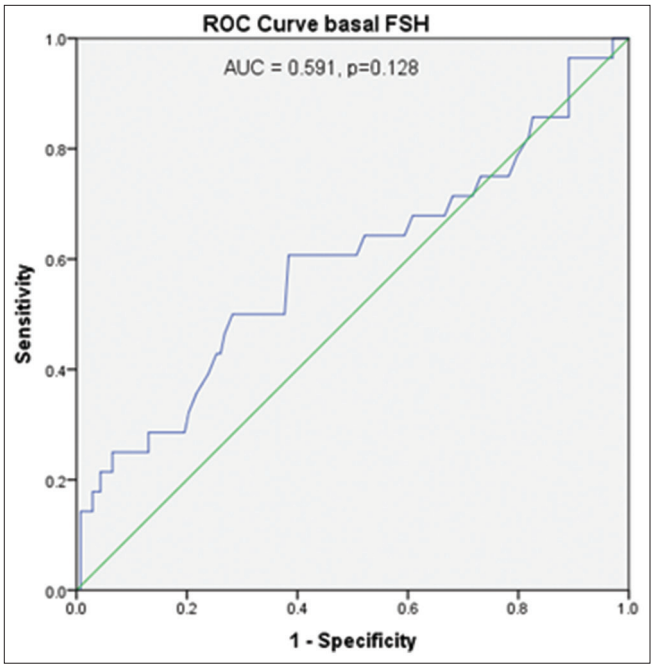

Figure 6: Basal FSH ROC curve for normal ovarian response. FSH: Follicle stimulating hormone, ROC: Receiver operating characteristics

$$n = \frac{P(1-P)\cdot\left(Z_{1-\alpha/2}\right)^2}{\partial^2}$$

where n = the desired sample size, Z = the standard normal deviation corresponding to 95% level of confidence. The value obtained from the normal distribution is 1.96, P = expected proportion or diagnostic sensitivity. The sensitivity of AFC for the detection of poor ovarian response was 89% from two studies.[12,13] P was therefore set at 90%. ∂ = degree of accuracy desired (i.e., precision) is set at 5% (0.05). The calculated

sample size n = 138. A 20% attrition rate was assumed, and the sample size was made up to 166.

Convenience sampling technique was used to select the 166 clients who met the inclusion criteria and gave a written informed consent that were recruited for the study. A brief history relating to the cause and duration of infertility was taken, weight and height were measured, and body mass index was calculated.

Transvaginal ultrasound scan was performed on all patients from day 2 to day 4 of a normal cycle. Those who had both ovaries clearly visualized with no evidence of polycystic ovarian disease or ovarian endometriosis had AFC assessment done. This was done by two medical personnel appropriately trained in transvaginal sonography who also had more than three years' experience in scanning. Both of them used the same general electric voluson E8 ultrasound system with 7 MHz transvaginal probe, real-time two-dimensional imaging. Interobserver coefficient of variation was kept below 5% by ensuring they followed the systematic process described by Broekmans.[14] Following the AFC assessment, on the same day, 10 ml of venous blood sample was obtained for the measurement of FSH. Samples collected are stored at a temperature of −2°C. Serum FSH was quantified with FSH Test Kit (ST AIA-Pack FSH) with the Automated Enzyme Immunoassay System AIA-360 manufactured by Tosho Corporation, Tokyo, Japan.

Controlled ovarian hyperstimulation was carried out by individualized antagonist protocol and the short agonist protocol. The antagonist protocol was used for younger women or women with higher AFC, while the short agonist protocol was used for old women or women with lower AFC. They received injection FSH (Gonal-f® by Merck Serono S.p.A Italy) or HMG (Menopur® by FERRING GmbH Germany) from day 3 of the cycle till trigger. Starting dose was individualized, ranging from 150 IU to no more than 450 IU, and increased after the second scan if the response was inadequate. The first scan for follicular tracking was done on day 6 and on alternate days until the human chorionic gonadotropin (HCG) trigger is administered. For the antagonist cycle, injection of cetrorelix acetate (Vestova® by BDR Pharmaceuticals Int'l Pvt. Ltd., India) 0.25 mg daily was commenced when the leading follicle was 12 mm, while for the agonist cycle, subcutaneous injection buserelin (Supercur® by Sanofi UK) 0.5 mg was commenced from day 2 or day 3 and are continued till HCG trigger was administered. When at least three leading follicles reach a diameter of ≥17 mm, 10,000 IU intramuscular injection of HCG (HUCOG® by Bharat Serums and Vaccines Limited India) would be administered and 34–36 h later, transvaginal ultrasound-controlled oocyte retrieval was performed under light sedation. Patients who had ≤3 follicles of ≥18 mm in diameter before HCG administration were considered to have an inadequate ovarian response for IVF, and their cycles were cancelled. Poor ovarian response was defined as ≤3 oocytes retrieved.

Data were collected structured proforma was administered by the researcher for data collection (Appendix II). Variables included the Subject's Unique ID, Ethnicity, Occupation, Education, Religion, Parity, weight, height, basal FSH levels (in mIU/ml), AFC, the total dose of human menopausal gonadotropin used (in IU), duration of stimulation (in days), counts of follicles ≥18 mm in diameter seen on the day of HCG administration and the number of oocytes retrieved. Statistical analysis was performed with SPSS software (version 21, Chicago, Illinois, USA). Continuous values were expressed in means and standard deviations, while categorical variables were presented in frequencies. Descriptive statistics of sociodemographic characteristics was done.

Sensitivity and specificity, the likelihood ratio of positive and negative tests, and positive and negative predictive values were derived for AFC and FSH tests. ROC curve, which is a plotting of the sensitivity or true positive rate against 1-specificity or false-positive rate at various threshold settings to determine which of the two tests (AFC or FSH) better predicts poor response. AUC was used to determine which of the two is the better predictor.

$P < 0.05$ was considered statistically significant for all statistical goodness-of-fit tests.

Results

A total of 1066 clients who met set criteria and gave consent were recruited into the study. The overall demographic and IVF characteristics are presented in Tables 1 and 2.

Table 1: Demographic characteristics of the clients (n=166)

Variables	Frequency (%)
Age group (years)	
20-24	11 (6.6)
25-29	37 (22.3)
30-34	60 (36.1)
35-39	52 (31.3)
40 and above	6 (3.6)
Parity	
Nullipara	98 (59.0)
Primipara	49 (29.5)
Multipara	19 (11.4)
BMI category	
Underweight	1 (0.6)
Normal	45 (27.1)
Overweight	63 (38.0)
Obese	57 (34.3)
Reason for IVF	
Male factor infertility	30 (18.1)
Tubal factor infertility	31 (18.7)
Unexplained infertility	101 (60.8)
Oocyte donation	2 (1.2)
PGD HBSS	1 (0.6)
Sex selection	1 (0.6)

BMI: Body mass index, IVF: *In-vitro* fertilization, PGD: Pre-implantation genetic diagnosis, HBSS: Sickle cell Haemogobin

Basal AFC was found to have a significant positive correlation with the number of oocytes retrieved. The correlation analysis showed a correlation coefficient (r) of 0.661 and a probability (P) < 0.0001 shown in [Figure 1]. This implies that the higher the basal AFC in the client, the higher the number of oocytes that will be retrieved. Basal FSH, on the other hand, showed a significant but weak negative correlation with the number of oocytes retrieved with $r = -0.211$, $P = 0.006$ shown in [Figure 2]. Another significant correlator with the number of oocytes retrieved was the age of the client, with a negative correlation $r = -0.517$, $P < 0.0001$ shown in [Figure 3]. The dose of HCG used also showed a significant positive correlation with the number of oocytes retrieved with $r = 0.454$ and $P < 0.0001$.

Twenty-eight (16.9%) clients were found to have poor responses as shown in [Figure 4]. Sixteen (9.6%) of the clients had cycle cancellation because they had <4 follicles above 17 mm before HCG. Of those that went on to have oocyte retrieval, 12 (5.3%) had ≤3 follicles retrieved.

The mean basal FSH for poor responders was 8.93 ± 3.97 mIU/ml, which was slightly higher than for normal responders, which was 7.61 ± 2.82 mIU/ml but not statistically significant ($P = 0.104$). The mean basal AFC for poor responders was 9.5 ± 4.15, which was significantly lower than for normal responders, with a mean of 12.76 ± 4.55 ($P = 0.001$).

The average duration of stimulation for poor responders was 10.82±1.18 days while for normal responders was 10.90±1.22 days which is not significantly different. The dose of HMG used was, however, significantly higher in the poor responders, who had an average of 3832 ± 1208 IU, while the normal responders had an average of 3145 ± 1257 IU ($P = 0.010$). This is shown in Table 3.

Table 2: *In-vitro* fertilization characteristics of the clients

Variables	Mean±SD
Basal FSH (mIU/mL)	7.837±3.0731
Basal AFC	12.21±4.642
Dose of HMG (IU)	3261.48±1286.88
Days of stimulation (days)	10.89±1.130
Follicles >17 mm before HCG	8.71±4.278
Number of oocytes retrieved	12.37±7.081

SD: Standard deviation, FSH: Follicle stimulating hormone, AFC: Antral follicle count, HMG: Human menopausal gonadotropin, HCG: Human chorionic gonadotropin

Table 3: Difference in baseline predictor variables between poor and normal responders

Parameter	Poor responders (n=28)	Normal responders (n=138)	P
Age (years)	35.21±4.29	31.75±4.59	<0.0001
AFC	9.5±4.15	12.76±4.55	0.001
FSH (mIU/mL)	8.93±3.97	7.61±2.82	0.104
Duration of stimulation (days)	10.82±1.18	10.90±1.22	0.743
Dose of gonadotropin (IU)	3832±1208	3145±1257	0.010

FSH: Follicle stimulating hormone, AFC: Antral follicle count

It was observed that for the prediction of poor response, basal AFC had the highest AUC with a value of 0.707 on the ROC curve shown in [Figure 5]. This implies that AFC has fairly high sensitivity and specificity for predicting poor ovarian response, and this finding was statistically significant ($P = 0.001$). Basal FSH had a lower AUC of 0.591 for the prediction of poor ovarian response on the ROC curve, but this was not statistically significant ($P = 0.128$) see [Figure 6].

Using the coordinates of the ROC curve, the cut-off values with the best combination of sensitivity and specificity for both AFC and FSH were determined, as presented in Table 4 below. The cut-off value for ≤10 for AFC had an accuracy of 67.47% in predicting poor response. Clients with AFC ≤10 are 3.4 times more likely to have poor responses compared to those that had AFC above 10, and this was statistically significant ($P = 0.005$). The cut-off value for poor response with basal FSH was ≥8.15 mIU/ml. This gave an accuracy of 61.45%, which was lower than that for AFC. Clients were 2.5 times more likely to have a poor response if their FSH was ≥8.15 mIU/ml, and this odd ratio was statistically significant ($P = 0.036$).

In Table 5, it is shown that the LR for the prediction of poor ovarian response (positive LR) and exclusion of poor ovarian response (Negative LR) were both in the nonvaluable test range.

A binary logistic regression to determine the relationship between predictors of poor response showed that the combination of variables did not significantly predict poor ovarian response, as depicted by the nonsignificant P values for the variables. However, when individual models were used, each had significant odds ratios for predicting poor response, as shown in Table 6.

Discussion

In this study, the value of basal AFC and basal FSH levels for predicting poor ovarian response was investigated in patients undergoing IVF treatment in a subset of the Nigerian population in Abuja.

The prevalence of poor ovarian response in the study population was 16.9%. Other studies have reported prevalence ranging from 8.2% to 25.5%[2,9,15,16] in various populations. Poor responders were significantly older women and had lower mean AFC. They had similar FSH, similar duration of stimulation, and higher doses of gonadotrophin. This trend was also similar to the figures quoted in the literature.[15]

Our data showed that the AFC of the patients had a moderate positive correlation with the number of oocytes retrieved ($r = 0.661$, $P < 0.0001$). This was within the range of values reported by other studies that had shown the correlation between AFC and the number of oocytes received, ranging between 0.431 and 0.757.[7,16-18]

Basal FSH, on the other hand, showed a weak but significant negative correlation with the number of oocytes retrieved

Table 4: Comparisons of diagnostic characteristics of predictors for poor ovarian response

Predictor	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	OR (95% CI)	*P*
Basal AFC	≤10	60.7	68.8	28.3	89.6	67.47	3.414 (1.475-7.906)	0.005
Basal FSH	≥8.15 (mIU/mL)	60.7	61.6	24.3	88.5	61.45	2.479 (1.078-5.698)	0.036

FSH: Follicle stimulating hormone, AFC: Antral follicle count, CI: Confidence interval, NPV: Negative predictive value, PPV: Positive predictive value, OR: Odds ratio

Table 5: Diagnostic usefulness in predicting poor ovarian response

Predictor	Cut-off value	LR + sensitivity/(1-specificity) (95% CI)	LR− (1-sensitivity)/(specificity) (95% CI)	Diagnostic usefulness
Basal AFC	≤10	1.95 (1.32-2.87)	0.57 (0.36-0.92)	Nonvaluable test
Basal FSH	≥8.15 (mIU/mL)	1.58 (1.10-2.28)	0.64 (0.40-1.03)	Nonvaluable test

FSH: Follicle stimulating hormone, AFC: Antral follicle count, CI: Confidence interval, LR: Likelihood ratios

Table 6: Logistic regression crude and adjusted odds ratios for predictors of poor ovarian response

Variables	Crude OR OR	95% CI for OR		*P*	Adjusted OR OR	95% CI for OR		*P*
		Lower	Upper			Lower	Upper	
AFC	0.824	0.734	0.925	0.001	0.881	0.772	1.006	0.061
FSH	1.131	1.001	1.278	0.047	1.050	0.927	1.189	0.445
Age	1.206	1.082	1.345	0.001	1.130	0.996	1.282	0.059

OR: Odds ratio, CI: Confidence interval, FSH: Follicle stimulating hormone, AFC: Antral follicle count

($r = -0.211$, $P = 0.006$). Its performance was obviously less than what was observed for AFC. Similarly, low values of correlation have also been reported in the literature.[19]

To compare the performances of AFC and FSH in predicting poor response, the ROC curve was used. The AUC for AFC was shown to be 0.707 (95% confidence interval [CI] 0.602, 0.812). This suggests a fair diagnostic accuracy for predicting poor ovarian response in our population. AUC reported in other studies has ranged between 0.664 and 0.93.[15,16,18,20] Our data showed that some patients who had high AFC had poor response to stimulation because were given lower doses of gonadotrophins to prevent the occurrence of ovarian hyper stimulation syndrome. This may have reduced the predictive ability of AFC and might have resulted in the moderate AUC 0.707 found in this study. It was found that in the subsequent cycle, when they had higher doses of gonadotrophin, their response was normal.

Basal FSH, on the other hand, was found to have an AUC of 0.591 (95% CI of 0.463, 0.719), which did not reach statistical significance in the prediction of poor ovarian response ($P = 0.128$). This showed that FSH is not a useful predictor of poor ovarian response in our population.

The ROC analysis for optimum cutoff for AFC in the prediction of poor ovarian response in this study was ≤10. This gave a sensitivity of 60.7%, specificity of 68.8%, PPV of 28.3%, NPV of 89.6%, and accuracy of 67.5%. This was the best combination of sensitivity from the range of possible cut-off values. Our data showed that the patients with AFC of ≤10 were 3.4 times more likely to have poor responses ($P = 0.005$). The optimum AFC cut-off for cancelled cycles reported in a study done in the United states was ≤10, which gave an AUC of 0.664 (95% CI 0.462, 0.866), sensitivity of 75%, specificity of 66.7%, PPV of 22%, and NPV 96%.[16] Their figures are very similar to the findings in our study and their mean AFC for poor responders was 9.4 ± 2.6, which was similar to the AFC of poor responders in our study, which was 9.5 ± 4.2. However, another study in Turkey gave a cut-off for AFC of 5.5 with a high AUC of 0.93, the sensitivity of 89%, and specificity of 87%.[15] This lower cut-off for AFC could be explained by a corresponding lower mean AFC for poor responders of 3.3 ± 2.4 found in their study. This suggests that the average AFC might vary in different populations of women, and the optimum cutoff for each population will vary as well.

On the other hand, the ROC analysis for optimum cutoff for FSH was ≥8.15 mIU/ml. This gave a sensitivity of 60.7%, specificity of 61.6%, PPV of 24.3%, NPV of 88.5%, and accuracy of 61.5%. The odds ratio for poor response at FSH ≥8.15 mIU/ml is 2.5 (95% CI 1.08, 5.7) and this reached statistical significance ($P = 0.036$). Literature have supported the findings in our study, suggesting that FSH ≥10 mIU/ml shows a high specificity of 80%–100% for predicting poor ovarian responses but low sensitivity of 10%–30%.[6] Literature is however replete with wide ranges of FSH,[21] which supports the poor predictive capabilities of FSH as a predictor of poor ovarian response.

The optimum cut-off points for AFC and FSH derived from the ROC analysis were subjected to likelihood ratio analysis to determine their diagnostic usefulness for the poor ovarian response. Basal AFC cut-off value of ≤10 had a positive likelihood ratio (LR+) of 1.95 (95% CI 1.32–2.87) and a negative likelihood ratio (LR−) of 0.57 (95% CI 0.36–0.92). Both LR fell in the range of nonvaluable tests, which suggests that the cut-off point would have a very low post-

test probability for making a diagnosis of poor ovarian response. This finding is similar to what was found in a study in the United Kingdom, where the positive likelihood ratio for AFC ≤10 was 1.9, with a 76% post-test probability for predicting poor ovarian response.[22] However, they did report that AFC of ≤4 had the highest positive likelihood ratio of 11.8 and post-test probability of 95%. This stands to reason as the lower the AFC cutoff used, the more diagnostic it would be for the poor ovarian response. This suggests that the cut-off value is useful as a predictor and not as a diagnostic test for the poor ovarian response. The positive and negative likelihood ratios for the cut-off point of FSH also performed similarly.

Our data showed that logistic regression that combined AFC, FSH, and age was not able to significantly predict poor ovarian response as none of the variables met statistical significance when combined to predict poor ovarian response. However, individually, their odds ratios were significant. Although each of the variables correlated significantly with the number of oocytes retrieved, they could not be used collectively to predict poor ovarian response. This is also supported by a study done in Turkey, which showed that the addition of other predictive variables to AFC did not improve its predictive value.[16]

Conclusion

This study has compared basal AFC and FSH for the prediction of poor ovarian response during IVF. Using the ROC analysis, basal AFC was shown to have an AUC of 0.707, which was significant and higher than the AUC for FSH of 0.591, which was not significant. The optimum cut-off values that give the best sensitivity and specificity for prediction of poor ovarian response was AFC ≤10 and FSH ≥8.15 mIU/ml. The accuracy of the AFC cut-off for the prediction of poor ovarian response was 67.47%, while for FSH was 61.45% which shows that the predictive accuracy of AFC was higher than that of FSH. Although the LR for this cut-off point suggest nonusefulness as a diagnostic test for the poor ovarian response, it could be a useful clinical guide in advising clients about their chances of poor response during IVF. Both correlation analysis and ROC curve analysis suggest that AFC is superior to FSH in predicting poor ovarian response. However, the cut-off point for FSH ≥8.15 mIU/ml reaches statistical significance for predicting poor ovarian response. This may also find usefulness in clinical practice.

Acknowledgment

Special appreciation to the assisted reproduction units of the Garki and Nisa Premier hospitals for their support in conducting this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Pelosi E, Forabosco A, Schlessinger D. Genetics of the ovarian reserve. Front Genet 2015;6:308.
2. Yang S, Chen X, Zhen X, Wang H, Ma C, Li R, *et al.* The prognosis of IVF in poor responders depending on the bologna criteria: A large sample retrospective study from China. Biomed Res Int 2015;2015:296173.
3. Jirge PR. Poor ovarian reserve. J Hum Reprod Sci 2016;9:63-9.
4. Pfeifer S, Butts S, Dumesic D, Fossum G, Giudice L, Gracia C, *et al*. Testing and interpreting measures of ovarian reserve: A committee opinion. Fertil Steril 2015;103:e9-17.
5. Hansen KR, Hodnett GM, Knowlton N, Craig LB. Correlation of ovarian reserve tests with histologically determined primordial follicle number. Fertil Steril 2011;95:170-5.
6. Moon KY, Kim H, Lee JY, Lee JR, Jee BC, Suh CS, *et al.* Nomogram to predict the number of oocytes retrieved in controlled ovarian stimulation. Clin Exp Reprod Med 2016;43:112-8.
7. Lonegro N, Napoli N, Pesce R, Chacón C. Antral follicle counts as a predictor of ovarian response. Rev Argent Radiol 2016;80:252-7.
8. Younis JS, Ben-Ami M, Ben-Shlomo I. The bologna criteria for poor ovarian response: A contemporary critical appraisal. J Ovarian Res 2015;8:76.
9. Scheffer GJ, Broekmans FJ, Looman CW, Blankenstein M, Fauser BC, teJong FH, *et al.* The number of antral follicles in normal women with proven fertility is the best reflection of reproductive age. Hum Reprod 2003;18:700-6.
10. Aday LA, Cornelius LJ. Designing and Conducting Health Surveys: A Comprehensive Guide. 3rd ed. San Francisco California: Jossey-Bass Publishers; 2006. p. 160.
11. Fosgate GT. Practical sample size calculations for surveillance and diagnostic investigations. J Vet Diagn Invest 2009;21:3-14.
12. Oliveira JB, Baruffi RL, Petersen CG, Mauri AL, Nascimento AM, Vagnini L, *et al.* A new ovarian response prediction index (ORPI): Implications for individualised controlled ovarian stimulation. Reprod Biol Endocrinol 2012;10:94.
13. de Carvalho BR, Rosa e Silva AC, Rosa e Silva JC, dos Reis RM, Ferriani RA, Silva de Sá MF. Ovarian reserve evaluation: State of the art. J Assist Reprod Genet 2008;25:311-22.
14. Broekmans FJ, de Ziegler D, Howles CM, Gougeon A, Trew G, Olivennes F. The antral follicle count: Practical recommendations for better standardization. Fertil Steril 2010;94:1044-51.
15. Mutlu MF, Erdem M, Erdem A, Yildiz S, Mutlu I, Arisoy O, *et al.* Antral follicle count determines poor ovarian response better than anti-müllerian hormone but age is the only predictor for live birth in *in vitro* fertilization cycles. J Assist Reprod Genet 2013;30:657-65.
16. Vrontikis A, Chang PL, Kovacs P, Lindheim SR. Antral follice counts (AFC) predict ovarian response and pregnancy outcomes in oocyte donation cycles. J Assist Reprod Genet 2010;27:383-9.
17. Lai Q, Chen C, Zhang Z, Zhang S, Yu Q, Yang P, *et al.* The significance of antral follicle size prior to stimulation in predicting ovarian response in a multiple dose GnRH antagonist protocol. Int J Clin Exp Pathol 2013;6:258-66.
18. Klinkert ER, Broekmans FJ, Looman CW, Habbema JD, te Velde ER. The antral follicle count is a better marker than basal follicle-stimulating hormone for the selection of older patients with acceptable pregnancy prospects after *in vitro* fertilization. Fertil Steril 2005;83:811-4.
19. Ng EH, Chan CC, Tang OS, Ho PC. Antral follicle count and FSH concentration after clomiphene citrate challenge test in the prediction of ovarian response during IVF treatment. Hum Reprod 2005;20:1647-54.
20. Bancsi LF, Broekmans FJ, Looman CW, Habbema JD, te Velde ER. Impact of repeated antral follicle counts on the prediction of poor ovarian response in women undergoing *in vitro* fertilization. Fertil Steril 2004;81:35-41.
21. De Castro EC, De Freitas Borges AL, De Rezende KN, Do Amaral WN. Antral follicle count in predicting appropriate dose of gonadotropin in *in vitro* fertilization cycles. Reprod Clim 2014;29:136-42.
22. Jayaprakasan K, Chan Y, Islam R, Haoula Z, Hopkisson J, Coomarasamy A, *et al.* Prediction of *in vitro* fertilization outcome at different antral follicle count thresholds in a prospective cohort of 1,012 women. Fertil Steril 2012;98:657-63.