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Pathology

Evaluation of Ovarian Response to Gonadotropin Stimulation, Oxidative Stress and Pregnancy Outcome among Nigerian Women Treated with In-Vitro Fertilization in Abuja

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Abstract **Original Research Article**

***Background and aim*:** Infertile couples are increasingly turning to Assisted Reproductive Technology (ART) for conception. Unfortunately, many of these women do not achieve clinical pregnancy and several factors such as hormonal imbalance, abnormal ovarian response, oxidative stress and senescence have been implicated. This study seeks to evaluate ovarian response to gonadotropin stimulation and the effect of oxidative stress and senescence on pregnancy outcome in women who enlisted in ART. ***Methods*:** A total of 46 women (mean age: 33.8±2.9 years and range 30-39) attending In-vitrofertilization (IVF) clinic at National Hospital Abuja were recruited for this study. Their blood specimens were collected four times at various stages during IVF treatment. Serum anti-mullerian hormone (AMH) was assayed using Cobas e411 auto-analyzer (ECLIA), total anti-oxidant status (TAS) was assayed using spectrophotometry method while Inhibin B was assayed using ELISA technique. Data was analyzed using Statistical Package for the Social Sciences software. ***Results*:** Twenty-two subjects 22/46(47.8%) were high responders, 11/46(23.9%) were normal responders, while 13/46(28.3%) were low responders to gonadotrophin stimulation after down regulation. The differences between the mean values of AMH across interval of sample collection days were statistically insignificant ($p>0.05$). The differences between the mean values of TAS and INHB across interval of sample collection days were statistically insignificant ($p>0.05$). There was a positive correlation ($r=0.443$, $p < 0.002$) between AMH and number of oocytes produced. A total of 16/46 (34.8%) of subjects were clinically pregnant while 30/46 (65.2%) achieved no pregnancy. ***Conclusion*:** Total Antioxidant Status and AMH levels appear to have affected pregnancy outcome. Therefore, TAS and AMH assays should be included as part of pre-IVF screening so as to improve pregnancy outcome in IVF treated women. ***Relevance for patients*:** This is a cross-sectional study of the response of subjects to gonadotropin stimulation, effect of oxidative stress and pregnancy outcome in women seeking conception via IVF method. The possible association between ovarian response to gonadotropin stimulation, effect of oxidative stress and pregnancy outcome may assist in the management of subjects seeking conception via IVF method.

Keywords: In-vitro fertilization, pregnancy outcome, oxidative stress, gonadotropins.

INTRODUCTION

Assisted reproduction and, in particular, the development of in-vitro fertilization (IVF) techniques has revolutionized the treatment of infertility (May-Panloup *et al*., 2016). Because IVF procedure is expensive with limited successful rate especially in low and medium income countries, attempts have been made to determine the factors which predict a successful outcome in a given patient or couple (Bozkurt *et al*., 2016). Fertility outcome with IVF is markedly low in women over 40 years old, presumably due to a decrease in ovarian reserve, which is a term that encompasses a decrease in both follicle number and oocyte quality. Since the advent of in vitro fertilization-embryo transfer (IVF-ET) in ART, controlled ovarian hyper-stimulation (COH) has gained acceptance and is widely used. However, women may respond differently to the dosage of gonadotropin (Gn), thus, resulting in different ovarian responses and hence different IVF pregnancy outcome (Begum *et al*., 2017). Poor ovarian responses to Gn stimulation will certainly result in a small number of oocytes collected and thus a small number of embryos available for transfer, which therefore reduces the success rate of IVF (Wilkosz *et al*., 2014). Conversely,

an excessive ovarian response to Gn stimulation increases the risk for ovarian hyper-stimulation syndrome (OHSS) (Seyhan *et al*., 2013). Worthy of note is the fact that diminished ovarian reserve and associated decline in reproductive potential onset is highly variable (May-Panloup *et al*., 2016). Inhibin B levels rise across the luteal follicular transition and peak in the mid-follicular phase, suggesting that they are secreted by the developing cohort of follicles, and may mark the number or quality of developing follicles at the baseline (Begum *et al*., 2017). Since it is being produced by the granulosa cells, inhibin B has been suggested as a direct biochemical marker of ovarian reserve and may prove to be useful adjunct in discriminating patients who are likely to respond to exogenous ovarian stimulation (Lawrenz *et al*., 2020). Anti-mullerian hormone serum measurements have recently been used mainly for the assessment of ovarian reserve (Iliodromiti and Nelson, 2013). The AMH type II receptor (AMH R II) has the capacity of binding only biologically active form of AMH (Di Clemente *et al*., 2010). Serum AMH levels have been shown to be fairly stable during the menstrual cycle with substantial fluctuations being observed in younger women (Al-Gubory *et al*., 2010a). Anti-mullerian hormone levels further demonstrate lower intra- and inter-cyclic variation than baseline FSH (Jamil *et al*., 2016). Clinical applications of AMH measurement have been proposed for a variety of indicators. Measurement of serum AMH is clinically used mainly for assessment of ovarian reserve reflecting the number of antral and pre-antral follicles, the so called antral follicle count (AFC) and for the prediction of response to controlled ovarian stimulation (La Marca *et al.*, 2014).

The commonest reasons attributed for the unsuccessful ART outcome are poor quality of germ cells or embryos, genital tract infections, uterine pathologies or endometrial receptivity or unsuitable ART method (Margalioth *et al.*, 2006; Schulte *et al.*, 2010; Fiedler and Ezcurra, 2012; Li and Jin, 2013). It is important to address other possible sources of inhibitions such as hormonal imbalance, abnormal ovarian response, oxidative stress and senescence to successful IVF outcomes. The study was therefore designed to evaluate total antioxidant status, ovarian reserve and response to gonadotropin stimulation in women who enlisted in ART.

MATERIALS AND METHODS

Study Population

Those recruited for this study were women between the ages of 30 – 49 years attending in-vitro fertilization (IVF) clinic at National Hospital Abuja. They cut across the major geographic zones of Nigeria.

Study Design:

This study is a cross-sectional study of infertile women seeking pregnancy by ART. It also employs both experimental and observatory study design.

Ethical approval

This study was approved by Health Research Ethics Committee (HREC) of National Hospital Abuja with reference number NHA/EC/006/2016. Strict confidentiality of participants' information were maintained. Participants individually signed a consent form after confirming their understanding of the contents of the consent form. Blood samples from participants were coded and adequately numbered.

Sample Size

Sample size calculation for repetitive and agreement studies:

The study was based on taking repetitive sample from the same group of patients, the formula for repetitive and agreement is most appropriate for this study based on the repetitive sampling of the same subjects for four times (Dell *et al.,* 2002). The modified Cohran formula (Kothari, 2004) for repetitive sampling was used. The minimum sample size for the study was 46.

Inclusion and Exclusion Criteria

Each participant in this study will have satisfied the following exclusion criteria;

Age: Women between 30-50 years were included while those below 30years and above 50years will be excluded.

Body Mass Index (BMI): Women must have a BMI of between 19 and 29.9 inclusive at the time of treatment. Those above 30 were excluded from the study.

Smoking status of both partners: Couples who smoke were not excluded from this study.

Cancer treatment: Women undergoing cancer treatment or whose partner is undergoing cancer treatment were also excluded from this study.

Previous sterilization: Couples are ineligible if previous sterilization has taken place (either partner), even if it has been reversed.

Blood Sample Collection Protocol

On day 3 of menses between the hours of 8:00am and 10:00am, 5mL of whole blood sample was collected into a plain sample tube (vacutainer), and labeled. Also, 14 days after commencing down regulation, between the hours of 8:00am and 10:00am 5mL of whole blood sample was obtained into a plain sample tube (vacutainer), and labeled. On the day of HCG injection (subcutaneous), that is after stimulation, 5mL of whole blood sample was collected into a plain sample tube (vacutainer), and labeled. Then 36 hours after HCG injection, another 5mL of blood sample was collected into plain sample tube (vacutainer), and labeled. All samples were allowed to stand for one hour, and then centrifuged at 2,000 revolutions per minute for 10 minutes after clot retraction. The sera were then

separated into plain tubes, labelled accordingly and stored at – 80 degree centigrade using In nova ultra-low temperature freezer until analyzed.

Anti-mullerian Hormone (AMH)

Cobas e 411 auto analyzers based on Electrochemilluminscence immunoassay (ECLIA) was used for the assay.

Human Inhb (Inhinbin B)

Elabscience kit was used on APDIA n.v Enzyme linked immunosorbent assay (ELISA) plate analyzer and washer machine.

Total Antioxidant Status

Method: Enzymatic colorimetric

Manual Procedure:

Into a reagent blank test tube, calibrator test tube, and sample test tubes, 800 µL of TAS buffer reagent were dispensed using semi-automatic pipette with disposable pipette tip. Exactly 50 µL of calibrator or sample were dispensed into the appropriate tubes. The initial absorbance A 1 was read at 660 nm using a 1 cm light path cuvette against reagent blank. Thereafter, 125µL TAS chromogen reagent was added to the blank, calibrator and sample test tubes. The complex were mixed thoroughly and incubated for 5 minutes at 37°C. Absorbance A2 was read at 660 nm.

Calculation

A2-A1 = ΔAbsorbance sample/calibrator/Blank

$$\text{Results (mmol/l)}: \frac{\Delta\text{Abs sample}}{\Delta\text{Abs Calibrator}} \times \text{Calibrator concentration}$$

Statistical Analysis

Data were entered and validated in Excel, 2010. All data analysis was performed using the Statistical Package for the Social Sciences software (version 20.0, IBM SPSS, Armonk, NY, USA). Comparisons of AMH, Inhibin B, and TAS, between various samples collection days, ovarian responses were performed using one-way analysis of variance (ANOVA). Comparison of AMH, Inhibin B, and TAS, between clinical pregnancy outcomes was done using independent Student t-test. The Pearson correlation coefficient was used to calculate the relationship between AMH, and Oocytes produced, and between AMH, oocytes and age of the woman. Variables were presented as mean ± Standard error of mean and $p<0.05$ was considered as statistical significant.

RESULTS

Table 1 shows the socio-demographic parameters of the study participants. The differences between the mean ages of the women (33.8 ± 1.09) and their spouses (43.3 ±1.24) were remarkable (p=0.02). The disparity in the level of education (p=0.01), type of job (p=0.002) and area of residence whether urban or rural were quite significant (p=0.0001).

Table 2 shows the mean and standard error of mean of the parameters of the interval of samples collection, the differences in AMH mean values on day 3 of menses, day 14 after commencing down-regulation and after gonadotrophin stimulation as well as the value at 36 hours after HCG Injection was statistically insignificant (p>0.05). Similarly, the differences between the mean values of TAS and INHB across interval of sample collection days were statistically insignificant (p>0.05).

Table 3 shows the pattern of response to gonadotropin stimulation among the women. An important aspect of this study was the evaluation of the measured parameters according to the responses of gonadotropin stimulation of the women. They were classified into high responders, normal responders and Low responders according to the number of oocytes produced. All the high gonadotropin responders had >11 oocytes with 16.77±0.91 oocytes mean values, normal responders oocytes ranged between 5-11 with 8.27±0.53 oocytes mean values, while low responders oocytes were <5 with 2.92±0.31 oocytes mean values. There was no statistical difference (p>0.05) in the age and BMI of the woman according to their category (responses to gonadotropin stimulation). The mean AMH value of higher responders was significantly higher (p<0.05) than those that were normal responders and low responders, and again no significant (p>0.05) difference was observed between the mean AMH values of the normal and low responder, The mean Inhibin-B value of higher responders was significantly lower (p<0.05) than those that were normal responders and low responders, and also, significant (p<0.05) difference was observed between the mean Inhibin-B values of the normal and low responder. The TAS did not show any significant mean differences according to the ovarian response as shown in table 2. The correlation between the values of TAS and oocytes showed a moderately positive statistical significant ((p<0.05) association across all the interval of blood samples collecting day, correlation between the values of TAS and INHB verse numbers of oocytes showed a negative insignificant (p>0.05) association within the blood sample collection days as shown in Table 3.

Table 4 shows Pearson correlation between measured parameters at the various days the blood samples were collected and number of oocytes produced. The correlation between the values of AMH and that of oocytes showed a positive significant relationship in all the blood sample collection days which were statistically significant (r- 0.443,p=0.002, r-0.457,p=0.001, r-0.452, p=0.002,r-0.36, p=0.002). However, other measured parameters did not show any significant correlation with the number of oocytes produced.

Table 5 shows the Comparison of measured parameters based on Clinical Pregnancy Outcomes among study participants. The difference in the mean serum AMH values in those women who had positive clinical pregnancy outcomes (2.88±0.61ng/mL) was significantly higher ($p<0.05$) than 1.53±0.27ng/mL in those women who had negative pregnancy outcome. The difference in the mean serum TAS values in women who had positive clinical pregnancy outcomes (1.56±0.13mmol/L) was significantly higher ($p<0.05$) than 1.17±0.0.08mmol/L in women who had negative pregnancy outcome, while that of inhibin-B was statistically insignificant according to pregnancy outcome in the study.

Table 1: Socio-demographic characteristics of studied population

Socio-demographic parameters	IVF-treated Women n=(46)	Men-Sperm Used n=46	X^2Cal(p-value)
Age group (yrs)			
30-35	28(60.9)	0(0.0)	
35-40	18(39.1)	35(76.1)	
>40	0(0.0)	11(23.9)	1.65(0.08)
Mean Age	33.8± 1.09	43.3± 1.24	2.30(0.02)
Age range	30-39	36-52	1.09(0.36)
Educational status			
Primary	3(6.5)	2(4.3)	
Secondary	6(13.0)	2(4.3)	
Tertiary	37(80.5)	42(91.4)	3.08(0.01)
Type of Job			
Civil Service	22(47.8)	6(13.0)	
Business	14(30.4)	32(69.6)	
unclassified	10(21.8)	8(17.4)	4.87(0.002)
Location of Residence			
Rural	2(4.3)	NA	
Urban	44(95.7)	NA	11.5(0.0001)

Keys, NA=Not Applicable, n=number, ( )%=percent, x^2= chi square

Table 2: Comparison of measured parameters at interval of Sample collection days (Mean and standard error)

Variables	INTERVAL OF SAMPLES COLLECTION					
	Day 3 of Menses Mean±SEM n=46	Day 14 after commenting Down-regulation Mean± SEM n=46	After Gonadotrophin stimulation Mean± SEM n=46	36 hours after HCG Injection Mean± SEM n=46	P-VALUE	Sig
AMH(ng/ml)	2.08±0.28[a]	2.11±0.28[a]	2.00±0.29[a]	2.06±0.28[a]	0.99	NS
TAS(mmol/l)	1.19±0..06[a]	1.23±0..06[a]	1.30±0..08[b]	1.37±0..07[c]	0.29	NS
INHB(pg/ml)	34.92±3.76[a]	35.81±3.86[b]	36.32±3.85[b]	35.17±3.71[b]	0.99	NS

Values are presented as means ±SEM. AMH= Anti-mullerian hormone; TAS= total antioxidant status; INHB=inhibin B; S=statistically significant, NS= Not Significant. Day3=Before Intervention, Day14= During Intervention, after gonadotrophin stimulation and 36hours after HCG injection=After Invention

Table 3: Parameters in women according to their response to Gonadotropin stimulation

Cycle Parameters	High responders n=22	Normal responders n=11	Low responders n=13
BMI(kg/m^2)	25.31±0.62[a]	24.65±1.28[a]	24.61±1.16[a]
Age(Years)	33.73±0.58[a]	33.82±0.89[a]	33.92±0.89[a]
Number of oocytes	16.77±0.91[a]	8.27±0.53[b]	2.92±0.31[c]
TAS (mmol/l)	1.23±0.34[a]	1.27±0.41[a]	1.46±0.28[a]
Inhibin-B(pg/ml)	30.50±1.34[a]	42.46±1.53[b]	41.00±2.10[c]
AMH(ng/mL)	2.77±0.45[a]	2.09±0.55[b]	0.62±0.24[c]

means ±SEM. Means in a row that do not share the same subscripts differ at $p<0.05$ in the Bonferroni comparison. AMH= Antimullerian hormone, TAS= total antioxidant status; INHB=inhibin

Table 4: Pearson Correlation between measured parameters values for the various blood samples collection days and Oocytes produced

Parameters	R-values	P-value
Oocytes vs AMH at day 3 of menses	0.443	0.002
Oocytes vs AMH at day 14 after commencing down regulation	0.457	0.001
Oocytes vs AMH after Gn stimulation	0.452	0.002
Oocytes vs AMH at 36hrs after HCG injection	0.36	0.002
Oocytes vs TAS at day 3 of menses	-0.025	0.871
Oocytes vs TAS at day 14 after commencing down regulation	-0.177	0.240
Oocytes vs TAS after Gn stimulation	-0.176	0.242
Oocytes vs TAS at 36hrs after HCG injection	-0.222	0.138
Oocytes vs INHB at day 3 of menses	-0.219	0.144
Oocytes vs INHB at day 14 after commencing down regulation	-0.212	0.157
Oocytes vs INHB after Gn stimulation	-0.236	0.114
Oocytes vs INHB at 36hrs after HCG injection	-0.228	0.127

Key: Gn=Gonadotrophin stimulation

Table 5: Comparison of measured parameters based on Clinical Pregnancy Outcomes

Parameter	Clinical Pregnancy Outcome	Mean	SEM	Levene's Test for Equality of Variances		
				t-value	P-value	Significant Level
AMH (ng/mL)	Positive n=16	2.88	0.61	2.323	0.03	S
	Negative n=30	1.53	0.27			
TAS (mmol/L)	Positive n=16	1.56	0.13	2.668	0.01	S
	Negative n=30	1.17	0.08			
Inhibin-B(pg/ml)	Positive n=16	36.81	1.48	0.98	0.52	NS
	Negative n=30	36.07	1.87			

Key: $p<0.05$ is statistically significant, while $p>0.05$ is not statistically significant. SEM=Standard Error of Mean, S=Statistically Significant, NS=Not Statistically Significant.

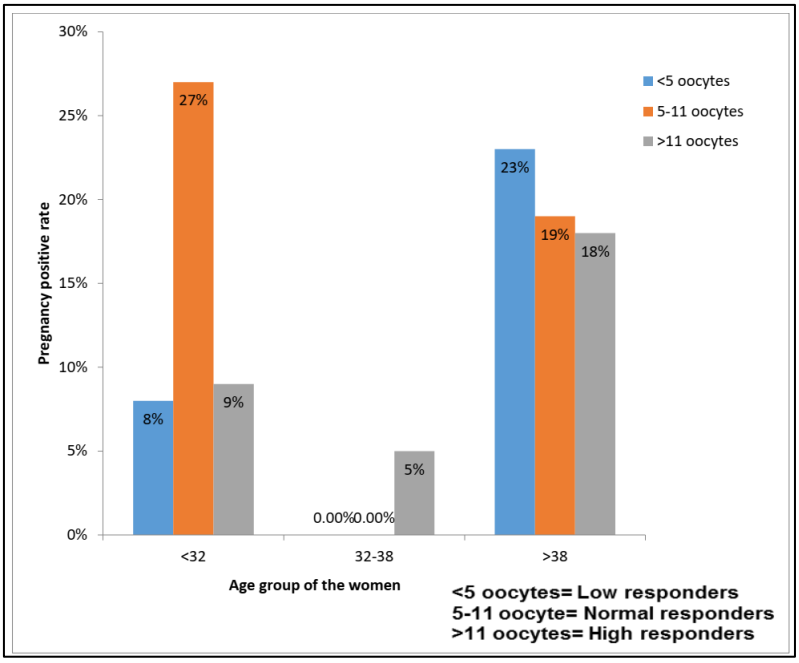

Fig 1: Relationship between the Women age and their ovarian responses against pregnancy positivity rate

Figure 1 shows the relationship between the age of the women and their ovarian responses by number of oocytes produced against pregnancy positivity rate. It was observed that among the relatively younger (aged <32 years), low, normal and higher responders accounted for 8%, 27%, and 9% positive clinical pregnancy outcome respectively while only 5% of the high responders show positive clinical pregnancy amongst the middle age participants (32 – 38 years). Positive clinical pregnancy of 23%, 19%, and 18% were observed amongst low, normal, and high responders in the older aged women (> 38 years).

DISCUSSION

Decreasing ovarian reserve is a major factor contributing to age related decline in reproductive potential (Ramalho de Carvalho *et al.*, 2012). Because ART involves multiple follicular developments in response to exogenous gonadotropins, chances of treatment success largely depend on the absolute number and functional capacity of follicles, which define ovarian reserve. An important aspect of decreased ovarian reserve is its onset variability. This being the situation, it therefore means that beside age, useful biomarkers of ovarian response to ovulation induction are needed for the prognostic assessment of ovarian reserve and so prediction of treatment outcome (Sandeep and Sangisapu, 2019). In the recent past, assessment of ovarian reserve relied wholly on indirect markers of ovarian function, such as follicle stimulating hormone, estradiol, FSH:LH ratio testing on the third day of the menstrual period as they require stimulation from either feedback inhibition or a stimulation loop. However, a direct measure of ovarian reserve is blood measurement of anti mullerian hormone (AMH) and Inhibin B (Moreno-Ortiz *et al*., 2018).

In this study, the observation of insignificant changes in the mean values of AMH at day 3 of menses, day 14 after commencing down regulation and on day after commencing down regulation, decrease on day after gonadotropin stimulation, and 36 hours after administering hCG across blood sample collection interval agrees with previous studies. It was reported by previous workers that AMH levels measured through a full menstrual cycle did not show consistent fluctuation patterns in contrast to levels of FSH, LH, and estradiol and that random fluctuations were small, indicating that AMH can be relied on as a non-cycle-independent marker for ovarian reserve (Marca *et al.*, (2006; Sandeep and Sangisapu, 2019). It was posited that serum AMH values are fairly constant through the normal menstrual cycle. However the observed slight fluctuation in serum AMH value under controlled ovarian stimulation (COS) could be as a result of the following; first, the decrease in AMH levels during COS could be as a result of the decrease in small antral follicles (Marca *et al.*, 2006). This study also showed that serum AMH significantly correlated with the decrease in the number of small antral follicles. The authors suggested that the serum AMH decrease during COS is possibly an indication of the reduction in the number of small antral follicles (McLennan and Pankhurst, 2017). Other investigators have also shown a relationship between serum AMH changes and small follicles with diameters of 2–5 mm. This could also possibly be as a result of the fact that standard and not individualized protocol of gonadotropin stimulation was used (van Tilborg *et al.*, 2016; Oliveira *et al.*, 2012). A previous study by Iglesias *et al*, (2014) indicated that doses without taking cognizance of racial disparity in ovarian response to gonadotropin stimulation could also be a possible reason for this observation. In their study where Indian and Spanish women were recruited for ART, they reported that irrespective of the fact that the difference in mean average age of the two groups was about 6 years (Indian 31.5 ±3.8 years Vs. Spanish 37.5 ±3.3 years), they had similar ovarian reserve markers (AFC and day 3 FSH) suggesting a 6-year advancement in ovarian aging. The fact that antral follicular count and day 3 FSH levels were similar but AMH was significantly lower in Indian women despite being 6 years younger and having received a significant higher amount of gonadotropins than the Spanish women, may reflect differences in early diagnostic capacity of diminished ovarian reserves. This is clearly a probable evidence of race disparity or the difference between chronological and biological ageing (Iglesias *et al*., 2014).

Follicular growth is modulated by AMH by inhibiting the recruitment of follicles from the primordial pool. This is achieved by modifying the FSH sensitivity of those follicles. AMH is considered to be reflective of the non - FSH dependent follicular growth. As a follicle matures, AMH production stops allowing the follicle to complete the development process during the FSH dependent stages of growth (Jamil *et al*., 2016). Over time, there is a steady decline in the level of AMH. This decline is as a result of decreasing number of follicles in the primordial pool (Bozkurt *et al*., 2016). The fact that AMH is secreted without dependence on other hormones, particularly the gonadotropins, and that AMH is expressed at a constant level, independent of cycle day makes AMH very attractive biomarker as a direct measurement of ovarian reserve (Dayal *et al*., 2014).

In this study, moderate positive statistical significant association ($r = 0.443$, $p= 0.002$), ($r = 0.457$, $p = 0.001$), ($r = 0.452$, $p = 0.002$), ($r = 0.360$, $p = 0.002$) between AMH values and oocytes retrieved across all the interval of blood sample collection days were observed. This observation agrees with previous works of Sandeep and Sangisapu, (2019). The result suggests that serum AMH value is a reliable predictor of number of oocytes retrieved and poor ovarian response. High ovarian responders to gonadotrophin stimulation have high AMH compared to low responders with low AMH value. This is a reflection of the amount of primordial follicles in the ovary hence a measure of the ovarian reserve. The

Levine's test for equality of variance of serum values of AMH between clinical pregnancy outcomes, indicates that the mean value of AMH for positive pregnancy was significantly higher ($p<0.03$) than values for negative pregnancy outcome. This shows that serum AMH value possibly has a direct bearing on pregnancy outcome in a controlled ovarian stimulation (COS) in ART treatment.

There was no statistical significant difference in Inhibin B values between clinically positive pregnant women and those who are negative. There was also no significant association between serum values of Inhinb B and number of oocytes retrieved. This observation is in agreement with a previous work which reported that Inhinb B serum concentration at commencement of ovarian stimulation with gonadotropin was not significantly different in pregnant and matched non pregnant cycles. This observation could possibly be due to the marked suppression of the ovarian function because of gonadotropin releasing hormone agonist treatment (Styer *et al*., 2015).

Data from this study shows that younger women who are normal responders experienced higher clinical positive pregnancy outcome than other age groups. This observation gives credence to the fact that age to a large extent has a marked effect on ovarian reserve and fertility (Wilkosz *et al*., 2014).

The significant increase in oxidative stress as noted from TAS values across the sample collecting days in this study, could be as a result of the effect of the gonadotropin used for stimulation of the ovary which could have exacerbated the production of reactive oxygen species (ROS) in reproductive tissues as a result of increased metabolism and steroidogenesis which then disrupts the body's antioxidant system, thus giving rise to oxidative stress (OS) (Kala *et al.*, 2017). Oxidative stress not only affect the quantity but also the quality of oocytes produced. Some authors also posited that for this same reason of increased metabolism during pregnancy, oxidative stress marker increases with age of the pregnancy except for pregnant women who are physically active (Idonije *et al*., 2011). Significantly higher OS was reported among women attending ART clinic in Lagos metropolis. The authors observed that OS may be a cause of poor ART outcomes in infertile women seeking intervention via ART, and that adequate intervention may ameliorate and improve the success rate of ART (Eromosele and Emokpae, 2020).

CONCLUSION

This study observed a strong correlation between the levels of AMH and the number of oocytes produced and also a significant association between the levels of TAS and clinical pregnancy outcomes as reduced antioxidant status were observed in poor responders and those women with low positive pregnancy outcome.

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