Original Article

Assisted Reproductive Technology: Experience from a Public Tertiary Institution in North Central Nigeria

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Abstract

Background: According to the World Health Organization, more than 180 million couples globally suffer from infertility, the majority being residents of developing countries. Assisted reproductive technologies (ARTs) offer a chance at parenthood to couples, who until recently would have had no hope of having a "biologically related" child. **Objectives:** This study aimed to determine pregnancy outcomes following assisted conception. **Materials and Methods:** This is a prospective study of 104 clients who underwent the procedure of ART between January 1, 2012 and December 31, 2016 at the ART unit of University of Ilorin Teaching Hospital, Ilorin, Nigeria. **Results:** Of the 510 clients who had infertility consultation at the ART clinic, 104 (20.4%) underwent ART procedures. The patients aged 27–46 years with a mean age of 33 ± 4.0 years. More than half (58.7%) had primary infertility. Their duration of infertility ranged from 1 to 20 years (4.6 ± 2.9 years). Majority (81.7%) had conventional *in vitro* fertilization while 19 (18.3%) had intracytoplasmic sperm injection. Thirteen (12.5%) cases of cycle cancellation and 11 (11.7%) cases of mild-to-moderate ovarian hyperstimulation syndrome were recorded. The clinical pregnancy rate per cycle started was 39.4%. However, 9/41 (22%) resulted in spontaneous miscarriages and 32 (6 sets of twin, 25 singleton, and 1 high-order multiple births) were successfully delivered, giving a live birth rate per cycle started of 30.8%. Pregnancy outcomes were not significantly affected by age of the women, types of infertility, and duration of infertility ($P > 0.05$). **Conclusion:** The outcomes of ART procedures in a resource-limited country like ours are encouraging. This underscores the need to encourage ART in public tertiary institutions in Nigeria through the support of government and nongovernmental organizations for the benefit of infertile couples who were hitherto hopeless.

Keywords: Assisted reproductive technology, experience, Nigeria, public tertiary institution

Introduction

According to the World Health Organization, infertility affects up to 10.5% of couples of reproductive age group globally[1] and 20% of couples of reproductive age group in Nigeria.[2] Its impact is particularly prominent in cultures where a high premium is placed on childbirth (as it is in Nigeria and many other African countries), leading to social, psychological, and economic challenges.[1,2]

The first pregnancy after *in vitro* fertilization (IVF) of a human egg and the first birth of an IVF child were reported in 1976 and 1978, respectively.[3,4] Since then, over five million births have been achieved worldwide by IVF and its modifications inclusive of contributions from developing countries like Nigeria.[5] Although advances in laboratory technology and clinical practice have permitted IVF to progress in low-resource setting like ours, it still remains out of reach of many infertile couples as the service is largely in private sectors,[6,7] not until recently that few public tertiary institutions[7,8] joined that offer relatively affordable IVF program. Therefore, this study is conducted to determine the pregnancy outcomes of assisted reproductive technology (ART) procedures in a tertiary public institution in a low-resource setting.

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Materials and Methods

This is a prospective study of 104 eligible clients who underwent assisted conception program, i.e., IVF/intracytoplasmic sperm injection (IVF/ICSI) treatment cycles in batches of 5–10 couples at the ART unit of University of Ilorin Teaching Hospital (UITH), Ilorin, between January 1, 2012 and December 31, 2016. Patients were recruited using purposive nonprobability sampling method. The case records of the patients were retrieved from ART unit/gynecological case notes and theater records. Data extracted from the case notes included bio-social variables, types of stimulation protocols, cycle cancellations, risk of ovarian hyperstimulation syndrome (OHSS), and pregnancy outcomes.

Informed consent was obtained from each patient, and protection of personal data and confidentiality were prioritized. Institutional Review Board approval was obtained, and the study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

A total of 104 clients were included in the study. All patients had a body mass index (calculated as weight in kilograms divided by the square of height in meters) ranging between 18 and 30 with a mean of 24 ± 4 kg/m^2. Their infertility evaluation results were normal. Seminal fluid analysis was conducted for male partners. The criteria for men were a sperm count of at least 20 million cells per milliliter of semen and progressive sperm motility (grades a + b) of 50% or greater. Male partners with semen count and/or motility less than the cutoff values were offered ICSI unless the sperm count was zero after centrifugation; therefore, donor sperm was used for IVF.

All clients consented to treatment before its commencement. In addition, all female partners had oral contraceptive pills for menstrual cycle synchronization and precervical assessment (trial/dummy transfer) on day 2/3 of menses prior to the commencement of stimulation.

Stimulation protocols

Two stimulation protocols were used for the study depending on the clinician's/patient's choice: The long agonist protocol with 60 clients and the antagonist protocol with 44 clients.

In long agonist protocol, patients received 0.5 mg daily buserelin (Suprecur®; Aventis Pharm, West Malling, UK) subcutaneously from day 21 of the cycle proceeding the synchronized cycle for 12–14 days. With the onset of menstrual cycle, the dose of Suprecur® was reduced to 0.25 mg daily till the day of trigger, and 150 IU (2 vials) of recombinant follicle-stimulating hormone (FSH) (Gonal F®; Merck Serono, Modugno (Bari), Italy) and 75 IU (1 vial) of highly purified FSH (Folliculin®; Barrat Pharmaceutical, Ambernath (E) India) were commenced on day 3 of menstrual cycle for 11–14 days.

Serial transvaginal ultrasonographic scan was done at interval from day 5/6 of stimulation to determine the number of follicles and endometrial thickness. Two hundred and fifty microgram (6000 IU) of recombinant human chorionic gonadotropin (hCG: Ovitrelle®; Merck Serono, Germany) trigger was administered subcutaneously whenever two or more follicles have grown to 18 mm or more, and oocyte retrieval was carried out at 35.5 h thereafter.

While in antagonist protocol, patients were commenced on 150 IU (2 vials) of recombinant FSH Gonal F (Gonal F®; Merck Serono, Germany) and 75 IU (1 vial) highly purified FSH (Folliculin®; Barrat Pharmaceutical, India) on day 3 of menstrual cycle for 11–14 days. Transvaginal ultrasonographic scan was also done at interval from day 5/6 of stimulation to determine the numbers, size of follicles, and endometrial thickness. Subcutaneous 2.5 mg daily gonadotropin-releasing hormone (GnRH) antagonist (Cetrotide®; Merck Serono, Germany) was administered whenever the follicles have grown to 14 mm size usually around day 6/7 of stimulation and was continued till the day of trigger to prevent premature luteinizing hormone surge. Eighty-three microgram (2000 IU) of recombinant hCG (Ovitrelle®; Merck Serono, Germany) and 0.25 mg of buserelin (Suprecur®; Aventis Pharm, West Malling, UK) were administered subcutaneously for trigger whenever two or more follicles have grown to 18 mm or more and oocyte retrieval was carried out at 35.5 h thereafter.

An excessive ovarian response (OHSS) risk was defined as 15 or more follicles 11–14 mm in diameter by days 10, 11, and 12 of controlled ovarian stimulation (COS), while a failed response was defined as no follicles after 10 days of COS, as the need to continue COS beyond 20 days.[9] Similarly, clients with failed response to stimulation, no oocyte at retrieval, failed fertilization, and no available embryos for transfer had their cycle cancelled.

Oocyte retrieval, insemination, embryo transfer, and luteal-phase support

Oocyte retrieval was done at about 35.5 h of hCG injection by the transvaginal needle aspiration under ultrasound guidance and was transferred immediately to the laboratory for oocyte screening and pickup. Mature oocytes were inseminated with prepared sperm after 6 h of oocyte pickup and were incubated. ICSI was done in cases of severe male factor infertility. Best cleavage embryos were transferred on day 5 of oocyte retrieval usually at the blastocyst stage using transabdominal ultrasound guidance, and the transfer catheters were checked to ensure that all the embryos were transferred. The number of embryos transferred (ET) was individualized using patients' age and experience from previous failed ART cycles, two or three in most cases. The luteal-phase support was conducted with progesterone (800 mg twice daily [Cyclogest pessaries®; Cox, Barnstaple, UK] and intramuscular 100 mg twice weekly [Gestone®; Ferring Pharmaceuticals, Mumbai, India]). Serum pregnancy test was carried out 2 weeks after ET and subsequently transvaginal ultrasound at 6th week for detection of gestational sac and/or viability of the fetus.

Statistical analysis

Statistical analysis was done using Epi Info version 7.1.3.0 (Centers for Disease Control and Prevention, Atlanta, USA). Categorical data were expressed as numbers and percentages while numerical data were expressed as mean and standard deviation. Associations of categorical variables were tested using Chi square test, while statistical significance was set at $P \leq 0.05$. Results were presented in tables.

Results

A total of 104 clients were recruited for the study. The patients aged 27–46 years with a mean age of 33 ± 4.0 years while their spouses aged 31–50 years with a mean age of 39 ± 4.7 years. More than half (58.7%) had primary infertility. Their duration of infertility ranged from 1 to 20 years (4.6 ± 2.9 years), with majority (96.2%) experienced 1–10 years of infertility [Table 1].

The cycle cancellation was 12.5%, incident of OHSS was 11%, and the mean number of oocytes retrieved and fertilized was 10.4 ± 6.0 and 6.9 ± 3.9, respectively. Also, the number of embryos transferred ranged from 1 to 3 [Table 2].

Table 3 shows the pregnancy outcomes. Forty-one pregnancies were recorded from 104 clients giving a pregnancy rate of 39.4% per cycle started, out of which 9/41 (22%) resulted in early first-trimester miscarriage and 32 were successfully delivered, giving a live birth rate of 30.8% per cycle started. Pregnancy outcomes were not significantly affected by age of the women, types of infertility, and duration of infertility ($P < 0.05$) [Table 4].

Table 1: Sociodemographic variables of clients (*n*=104)

Variables	Frequency (%)	Range	Mean
Age (years)			
25-34	69 (66.3)	27-46	33±4.0
35-44	33 (31.7)		
≥45	2 (1.92)		
Age (spouse)			
30-39	62 (59.6)	31-50	38.9±4.7
40-49	39 (37.5)		
≥50	3 (2.9)		
Type of infertility			
Primary	61 (58.65)		
Secondary	43 (41.35)		
Duration of infertility (years)			
1-10	100 (96.15)	1-20	4.6±2.9
11-20	4 (3.85)		

Table 2: Clinical results (*n*=104)

Variables	Frequency (%)
Number of oocytes retrieved (mean)	10.4±6.0
0	8 (7.7)
1-10	51 (49.0)
11-20	38 (36.5)
21-30	7 (6.7)
Number of oocytes fertilized (mean)	6.9±3.9
0	8 (7.7)
1-10	81 (77.9)
11-20	15 (14.4)
Number of embryos transferred (*n*=91)	
1	9 (9.9)
2	25 (27.5)
3	57 (62.6)
Cycle cancellation	
Yes	13 (12.5)
No	91 (87.5)
OHSS	
Yes	11 (11.7)
No	83 (88.3)

OHSS: Ovarian hyperstimulation syndrome

Discussion

The clinical pregnancy rate in this study was 41/104 (39.4%), this is however slightly higher than 180/600 (30%)[8] and 31/115 (27%)[6] reported in Benin and Nnewi in southwestern and eastern Nigeria, respectively. This may be attributed to the smaller sample size of our study population as against previous studies.[6,8] Furthermore, achieving competence and capacity on ICSI for insemination in severe oligospermic male partner and the use of donor sperm in azoospermic male partner could be contributory.

In addition, the live birth rate of 30.8% in our series is higher than 16.2%[8] and 18.3%[6] reported in similar studies in Nigeria while the miscarriage rate of 22% (of those who became pregnant) is comparable with 21.9%[10] reported in Philadelphia, USA, but far higher than findings of 6.6%[8] and 8.7%[6] obtained in Benin and Nnewi, Nigeria, respectively. In the absence of national legislation as regards the number of ET, the maximum number of embryos transferred in this study was three as against elective single ET policy[11] in most European countries[12] due to paucity of facilities to conduct advanced screening of embryos prior to transfer with resultant prevalence of multiple births of 6/104 (5.8%) which is comparable to 36/600 (6%) reported by Orhue *et al*.[8]

In this study, the prevalence of OHSS was 11.7%, all were mild OHSS that did not warrant cycle cancellation and majority (9 out of 11) resulted from GnRH agonist stimulation protocol. This is, however, lower than OHSS episode of 15% reported in a previous study in Benin, Nigeria.[8] The findings of lower OHSS episode in GnRH antagonist stimulation protocol as against GnRH agonist stimulation protocol are in keeping with findings from previous studies.[13-15] Furthermore, the cycle cancellation rate of 12.5% resulted from poor ovarian response and failed fertilization involving five and eight clients, respectively, with the majority, i.e., three and seven, respectively, resulted from GnRH agonist stimulation protocol. This is inconsonance with the findings of Craft *et al*.[16] where a significantly higher cycle cancellation rate was observed in GnRH agonist stimulation protocol compared with GnRH antagonist stimulation protocol.

Table 3: Obstetric outcomes

Variables	Frequency (%)
Clinical pregnancy	41/104 (39.4)
Live birth	32/104 (30.8)
Multiple pregnancies	6/104 (5.8)
Miscarriages (among those pregnant)	9/41 (22)

Table 4: Relationship between sociodemographic variables and *in vitro* fertilization outcome

Variables	Pregnancy outcome		χ^2	df	*P*
	Pregnant	Not pregnant			
Age (years)					
25-34	25	44	19.4	32	0.961
35-44	15	18			
≥45	1	1			
Type of infertility					
Primary	34	27	3.30	4	0.508
Secondary	29	14			
Duration of infertility					
1-10	38	62	14.9	26	0.960
11-20	3	1			

Our cycle cancellation rate of 12.5% is higher than 8.1%[7] reported in an earlier study within the same facility but slightly lower than 16% reported in Benin, Nigeria.[8]

The age-related decline in female fecundity and fecund ability has been well documented in both natural and artificial reproduction[17] and probably results from a combination of progressive follicular depletion, decline in granulose function, poor oocyte quality, and reduced endometrial receptivity.[18] On the contrary, we obtained an insignificant association between pregnancy outcomes, age of the women, types of infertility, and duration of infertility. This may be related to the limited sample size in this study. This finding is in keeping with the results of an earlier report in the same institution.[7]

Conclusion

The clinical pregnancy and live birth rates of ART in UITH Ilorin are 39.4% and 30.8%, respectively. This has enabled couples to fulfill their parental desires who previously do not have the hope of becoming parents. Thus, there is a need to encourage ART in public tertiary institutions in Nigeria for the benefit of teeming population of affected citizenry who were hitherto hopeless.

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Conflicts of interest

There are no conflicts of interest.

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