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A Review of Pregnancy Outcomes following Intrauterine insemination for Infertile Women at a Public Health Facility in Ilorin, Nigeria.

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Abstract

Introduction: Infertility is a problem of public health importance in Nigeria and many other developing nations because of its high prevalence and its serious social implications on affected couples and families. Of the various treatment options available for the treatment of infertility, intrauterine insemination is a viable option with appreciable success rate. The study aimed to determine pregnancy outcomes following intrauterine insemination.

Materials and Methods: Twenty one (21) clients who underwent the procedure of Intrauterine insemination between 1st January 2012 and 31st December 2013 at the Assisted Reproduction Technology (ART) unit of University of Ilorin Teaching Hospital, Ilorin, Nigeria.

Results: The patients aged 26-40 years with a mean age of 32.1 ± 3.9 year. Nine (42.9%) had primary infertility while 12 (57.1%) had secondary infertility. Their duration of infertility ranged from 1 to 8 years (4.3 ± 2 years). Two (9.5%) had Artificial Insemination by donor's semen (AID). Nine clinical pregnancies were recorded giving a cumulative pregnancy rate of 42.9%. However 5 (55.6%) resulted in early first trimester miscarriage and of the remaining four pregnancies, one woman successfully delivered, giving a live birth rate of 25%. Pregnancy outcome was not significantly affected by age of the woman, husband age, social class, types and duration of infertility ($p > 0.01$).

Conclusion: Intrauterine insemination is one of the mainstays of therapy for couples suffering from various forms of infertility prior to embarking upon the more expensive in vitro fertilization procedures. Thus the need for proper patient selection to increase pregnancy rates from the procedure.

Key words: Intrauterine insemination, infertility, assisted reproduction technology.

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Introduction

Intrauterine insemination (IUI), an assisted reproductive technique widely used for infertility treatment all over the world, is a distinguished method which is cheaper and less invasive compared to other assisted

reproductive techniques¹. It is usually selected as a first treatment option for infertile couples with patent tubes, cervical mucus hostility, mild endometriosis, or mild or moderate male factor infertility or as empirical treatment in unexplained infertility².

It involves the insertion of sperm into the women's uterus with the aid of a fine plastic tube that is passed through the cervix and into uterus¹. The procedure is timed to coincide with the release of an egg or eggs (ovulation) in a natural or a stimulated cycle. Ultrasound and hormonal analysis are used to monitor progress throughout the treatment. If successful, fertilization takes place in the uterus¹.

The overall success of IUI varies, with pregnancy rates ranging from 2.7% to 66%^{1,4,5}. Frequent problems in evaluating success rates of this treatment may be due to variability in bio-social variables of selected subjects, aetiology and duration of infertility, difference in ovarian stimulation protocols⁶, timing and frequency of insemination, number of treatment cycles and total number of motile sperm inseminated¹. Although, the results may appear the same for some of these factors, a lack of consistency is being reported for others, such as gender fertility factor and husband age^{1,8}.

The objective of this observational study was to determine the bio-social characteristics, pregnancy outcomes and identify the variables that contribute to the success of IUI procedure in our centre.

Materials and Methods

This is a prospective study of patients who underwent IUI procedure at ART unit of the department of Obstetrics and Gynaecology, University of Ilorin Teaching Hospital, Ilorin from 1st of January to 31st December 2013.

Information on biosocial data and other general information of the patients were documented at presentation. All female partners had undergone diagnostic work-up including hysterosalpingography / laparoscopy + dye test, transvaginal ultrasonography and measurement of baseline levels of follicle-stimulating hormone (FSH), leutinizing hormone (LH),

oestradiol, thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), prolactin, and day 21 progesterone. Male factor evaluation included uro-andrologic examination, measurement of baseline levels of FSH, LH, testosterone, TSH, T3 and T4. Male infertility was diagnosed when sperm abnormalities according to World Health Organization (WHO) criteria⁹ were seen in at least 2 semen samples.

Semen samples were obtained from male partner of couples who were undergoing IUI treatment for infertility through masturbation after 3-7 days of sexual abstinence. After liquefaction at room temperature for 30 minutes, the semen samples were examined under a microscope to define their characteristics regarding concentration, motility and morphology. Then, semen was washed with an Earle's Balanced Salt Solution (EBSS) - containing medium (Ferticult, Beernem, Belgium) at 350 x g for 10 minutes. The pellet underwent centrifugation on a mini-Percoll gradient (40% to 80%) at 200 x g for 20 minutes. Ninety-five percent of the fraction was recovered and washed again with EBSS-containing medium at 350 x g for 5 minutes. The pellet was resuspended to 1 mL, and then post wash motility and motile sperm count were reassessed. Finally, the sample was centrifuged again, and the pellet resuspended to 0.3 mL and was left for incubation at 37°C. The final volume for insemination was 0.5 mL.

All women in the study underwent ovarian stimulation using clomiphene citrate (Clomifen; Leiras, Tampere, Finland) and /or human menopausal gonadotrophin (HMG)/human chorionic gonadotrophin (HCG) (Pergonal; Serono, Aubonne, Switzerland). For clomiphene citrate -stimulated cycles, 100mg clomiphene citrate was given between days 2 and 6. For clomiphene citrate plus gonadotrophin stimulation, 100mg clomiphene citrate was given between days 2 and 6, followed by 150IU of gonadotrophins added on days 6, 9 and 12.

Follicular maturation, ovarian and endometrial responses were monitored by serial transvaginal ultrasonography on cycle days 9 to 13 and 5000-10000IU of HCG (Pregnyl; Organon or Profasi; Serono) was administered when at least one follicle was > 16mm in mean diameter and standard IUI was scheduled 36 h after administration of HCG^{7,8}.

Intrauterine insemination was performed using intrauterine catheter (Kremer Delafontaine; Prodimed, Neuilly-en-Thelle, France) with a 1ml syringe. The catheter was gently passed through the cervical canal and the sperm suspension expelled into the uterine cavity. All techniques were carried out using sterile procedure. The IUI was performed with the patient in the dorsal lithotomy position. The women remained supine for 30 minutes after IUI. After insemination, each patient received progesterone (400mg vaginal suppository twice daily and 100mg intramuscularly twice weekly), followed as the same dosage after pregnancy confirmation for 14 weeks.

Pregnancy confirmation was done on the 2nd and 3rd weeks after IUI using serum β -hCG level. In pregnant women, luteal phase support was

continued until 14 weeks of gestation while those with negative findings luteal support was stopped for menses to return. Clinical pregnancy was defined as transvaginal ultrasonographic visualization of intrauterine gestational sac (s).

Data entry was done with the help of structured codes in Microsoft Excel. Data validation was done to check for errors in data entry. Descriptive statistical analysis was carried using a commercial statistical package (SPSS/PC version 16.0, SPSS Inc., Chicago, III, USA). A p-value of < 0.05 was considered as statistically significant.

Results

Out of 132 patients who had infertility consultation at the ART clinic, 21 (15.9%) underwent successful intrauterine insemination procedures. The patients aged 26-40 years with a mean age of 32.1 ± 3.9 year. Seventeen (81%) out of twenty one were nulliparous and majority (71.4%) belong to middle social class. The mean age of their husband was (37.4 ± 4.3) . Nine (42.9%) had primary infertility while 12 (57.1%) had secondary infertility. Their duration of infertility ranged from 1 to 8 years (4.3 ± 2 years). About one-third (33.3%) had Polycystic Ovarian Syndrome (PCOS).

Table 1: Socio-demographic characteristics

Variable	Frequency	Percentage (%)	p value
N=21			
Age wife (years)			
26-30	9	42.9	
31-35	8	38.1	
35-39	2	9.5	
>40	2	9.5	
Range-26-40 years,			
Parity		mean=32.1±3.9	
0	17	80.9	
1	2	19.1	
mean= 0.191±0.402; median= 0.00			
Age husband (years)			
31-35	10	47.6	
36-40	6	28.6	
41-45	4	19.0	0.003
>45	1	4.8	
Range-31-47 years		mean=37.4±4.3	
Social Class			
Low	6	28.6	
Middle	15	71.4	
Type of infertility			
Primary	9	42.9	
Secondary	12	57.1	
Duration of infertility (years)			
1-3	9	42.9	
4-6	9	42.9	
7-9	3	14.2	
Range= 1-8 years		mean=4.3±2.0	

Table 2: *Gender infertility/ Tubal factors/ Semen Analysis/ Hormonal profile/ IUI Procedure/ Outcome*

Variables	Frequency	Percentage (%) N=21
Gender-Infertility factor		
Male factor	2	9.5
Female factor	7	33.3
Unexplained	12	57.1
Tubal factors		
Bilateral patent tube	21	100
Sperm counts		
Normospermia	19	90.5
Severe oligospermia	1	9.5
Hormonal profile		
Hypergonadism	2	9.5
Hypogonadism	5	23.8
Normogonadism	14	66.7
Prolactin		
Normoprolactinaemia	17	81.0
Hyperprolactinaemia	4	19.0
Types of IUI Procedure		
IUI-H	19	90.5
AID	2	9.5
Pregnancy outcomes		
Outcome (21)		
None	12	57.1
Pregnancy	9	42.9
Miscarriages (n=9)		
Yes	5	55.6
No	4	44.4

Table 2 showed gender infertility factors, investigation results, types of IUI procedures and pregnancy outcomes. Male alone factor and female alone factors accounted for 2(9.5%) and 7 (33.3%) of cases respectively. More than half (51.7%) had unexplained infertility. All female alone factors were as a result of ovulatory disturbances secondary to PCOS. All had bilateral patent tubes. Majority (90.5%) of their

spouse had normozoospermia except for 2 (9.5%) that had severe oligospermia. Most women (66.7%) had normogonadotrophic normogonadism with less than one-third (19.0%) having hyperprolactinaemia. Majority (90.5%) had Homologous intrauterine insemination (IUI-H), while 2 (9.5%) had Artificial insemination Donor (AID).

Table 3 showed pregnancy outcomes following

IUI procedures. Out of 21 patients that underwent IUI, nine (9) clinical pregnancies were achieved giving a cumulative pregnancy rate of 42.9%. However 5(55.6%) resulted in early first trimester miscarriage and of the remaining four pregnancies, one woman

successfully delivered, giving a live birth rate of 25%, while others are on-going. Pregnancy outcome was not significantly affected by age of the woman, husband age, social class, types and duration of infertility ($p > 0.01$)

Table 3: Socio-demographic variables and pregnancy outcome

Variables	Pregnancy outcome		χ^2	OR	95%CI	p value
	Yes (%)	No (%)				
Age wife (years)						
26-35	5(29.4)	12(70.6)	0.62	0.42	0.03-5.93	0.574*
>35	2(50.0)	2(50.0)				
Age husband (years)						
31-40	4(25.0)	12(75.0)	2.10	0.22	0.02-2.64	0.280*
>40	3(60.0)	2(40.0)				
Parity						
0	5(29.4)	12(70.6)	0.62	0.42	0.03-5.93	0.574*
1	2(50.0)	2(50.0)				
Social Class						
Low	3(50.0)	3(50.0)	1.05	2.75	0.27-31.37	0.354*
Middle	4(26.7)	11(73.3)				
Duration infertility (years)						
≤ 3	4(44.4)	5(55.6)	0.88	2.40	0.27-23.27	0.397*
>3	3(25.0)	9(75.0)				
Type of infertility						
Primary	0(0.0)	9(100.0)	7.88	0.00	0.00-0.68	0.007*
Secondary	7(58.3)	5(41.7)				

*Fisher exact

Discussion

The cumulative pregnancy rate in this study was 42.9%. This is far higher than the lowest rate of 2.7%; but slightly lower than the highest rate of 66% reported in previous studies^{1,4,5}. This may be attributed to the fact that majority of the patients recruited for this study were below 40

years of age as fecundity and fecund ability are age dependent⁹.

Also, the rate of evolutive pregnancy of 44.4% (pregnancies which did not miscarry) obtained in this study is comparable to 50%¹⁰, 54%¹¹ and 68%¹² respectively obtained from several studies. However, it is lower than 88% reported by

Shahrzad et al¹. These differences may be due to variations in ovarian stimulation protocols, methods of semen preparation and sample size of these studies. In this study low-cost ovarian stimulation (use of clomiphene citrate and HMG) and density gradient semen preparation were adopted.

We found that the majority of pregnancies 8 (88.9%) recorded from this study were from women age < 40 years though the difference was not statistically significant. The age related decline in female fecundity has been well documented in every aspect of natural and artificial reproduction and probably results from a combination of progressive follicular depletion, decline in granulosa function, poor oocyte quality and reduced endometrial receptivity¹.

Multiple pregnancies with its attendant medical and socio-economic sequel is an important aspect that needs to be considered when ART is evaluated with a reported incidence of 6.5-25%^{13, 14}. However, multiple gestations seem to be less frequent following IUI compared with generally reported in in vitro fertilization and intracytoplasmic sperm injection (ICSI) (25-30%)¹⁴. In our study all the pregnancies recorded were singletons.

In conclusion, our results suggest low-cost ovarian stimulation using clomiphene citrate and HMG for intrauterine insemination is a useful treatment for infertile couple younger than 35 years of age most especially in the developing countries like ours. Thus, we believe that our results may be helpful for better counseling and selection of couples undergoing infertility treatment, thereby increasing the success of IUI therapy before opting for much more expensive invasive assisted reproductive treatments.

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