AN EVALUATION OF COUPLES UNDERGOING INTRAUTERINE INSEMINATION IN A CLINIC IN JOHANNESBURG

A research report submitted to the Faculty of Hearth Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Masters in Medicine (MMed)

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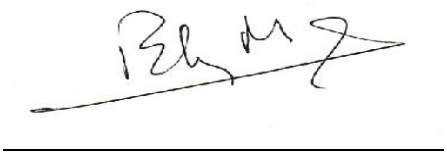
Johannesburg 2024

DECLARATION

I, Mulema Noel FETI declare that this work is an original research report and it has not been submitted before for any degree or examination at any other University.

It is being submitted for the Degree of Master of Medicine in the branch of Obstetrics and Gynaecology at the University of the Witwatersrand, Johannesburg.



Mulema Noel FETI

30th day of April 2024 at Johannesburg

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TABLE OF CONTENTS

LIST OF TABLES

ABBREVIATIONS

ART	Assisted Reproductive Techniques
BMI	Body Mass Index
CC	Clomiphene Citrate
CPR	Clinical Pregnancy Rate
FSH	Follicle Stimulating Hormone
HCG	Human Chorionic Gonadotropin
HIV	Human Immunodeficiency Virus
HMG	Human Menopausal Gonadotropin
IUI	Intrauterine Insemination
IVF	In Vitro Fertilization
LH	Luteinizing Hormone
OI	Ovulation Induction
TMSC	Total Motile Sperm Count
WHO	World Health Organization

ARTICLE

An Evaluation of Couples undergoing Intrauterine Insemination in a Clinic in Johannesburg

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ABSTRACT

Background: Infertility is a common reason for consultation in Gynaecology. Most cases of infertility can be treated with assisted reproductive techniques (ART). However, assisted reproductive therapy is still largely unavailable or inaccessible in most low- and middle-income countries. Intrauterine insemination (IUI), which consists of the deposition of processed sperm from the partner or donor into the cavity of the uterus around ovulation time, is one of the oldest methods.

Objective: To describe couples who underwent IUI and determine predictors of successful IUI.

Methods: A retrospective descriptive study of all couples who underwent IUI at the BioArt Fertility Centre in Johannesburg from January 2019 to June 2021. In total, 451 IUI cycles were analysed in 273 couples. The main outcome measure was a positive serum quantitative pregnancy test 14 days after IUI. Multivariate logistic regression was done to find predictors of successful IUI.

Results: The mean male age was 37.15 years (SD±5.16) with most male participants having a processed total motile sperm count (PTMSC) of > 39 x 10^6/ml. The mean female age was 33.51 years (SD±4.83). Most females had primary infertility, and the median duration of infertility was three years. The main etiology of infertility was ovulatory dysfunction (37.7%). The overall pregnancy rate per cycle was 13.1%, comprising 56 clinical and three biochemical pregnancies. Letrozole was the main ovarian stimulation agent (86%). The PTMSC, female age, duration of infertility, and follicle size significantly increased the pregnancy rate with p-value <0.05.

Conclusion: IUI is an effective choice of therapy for infertility in selected couples, achieving acceptable pregnancy rates for up to three treatment cycles, especially in females < 40 years with less than five years' duration of infertility, and in males with a PTMSC of > 39 x 10^6/ml.

Keywords: intrauterine insemination, infertility, pregnancy rate

INTRODUCTION

Infertility in couples is one of the common reasons for consultation in Gynaecology, and it is defined as a condition of the male or female system of reproduction characterized by the failure to achieve a clinical pregnancy after twelve months or more of regular unprotected sexual intercourse according to the World Health Organization (WHO) [1]. Infertility is described by the American College of Obstetrics and Gynaecology (ACOG) as an inability to achieve clinical pregnancy within twelve months of unprotected sexual activity or therapeutic donor insemination in women under the age of 35 or within six months in women older than 35 years [2].

Globally, about 12−15% of couples fail to conceive after a one-year period of trying. In South Africa, infertility affects 15−20% of the population, i.e., one in every six couples [3]. Identifying the etiologies of infertility will allow us to properly address this public health problem, which, according to the 2020 WHO report, affects more than 48 million couples worldwide [1]. Infertility can be due to female factors in approximately 35% of cases, in 30% to male factors, in 20% to combined factors, and in 15% remains unexplained [4]. With ART, namely, intrauterine insemination (IUI), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI), the majority of infertility cases can be treated. However, these methods are still largely unavailable or inaccessible in most low- and middle-income countries (LMICs) [5].

IUI, which consists of the deposition of processed sperm from the partner or donor into the cavity of the uterus around ovulation time, is one of the oldest methods of assisted reproductive techniques and is still widely used to this day due to the advantage of it being simple and less expensive compared to other methods. IUI can be done in natural or stimulated cycles. This technique is the first option of treatment for couples with ovulatory dysfunction, cervix related infertility, mild endometriosis, unexplained infertility and male subfertility. IUI is also used in cases of sexual dysfunction, same-sex couple's infertility using donor sperm, and for safe conception in an HIV-discordant couple [5].

According to the literature, the success rate of this procedure is around 5−20% per cycle [6], depending on the cause of infertility [7]. It has also been reported that the success of IUI depends on a number of parameters, including the female profile (age, BMI), the duration and type of infertility, the regimen of stimulation, the ovarian response, the thickness of the

endometrium, the number of IUIs, the percentage of sperm with normal morphology, and processed total motile sperm count (PTMSC) [8].

The purpose of the study was to describe couples who underwent IUI and determine the predictors that contribute to successful pregnancy following IUI.

MATERIALS AND METHODS

Participants

During this retrospective descriptive study, we evaluated a total of 451 IUI cycles from January 2019 until June 2021 at the BioArt Fertility Centre in Johannesburg. This study has been cleared and approved by the Human Research Ethics Committee of the University of the Witwatersrand and it was conducted with the consent of all participants (Clearance certificate No. M211017). All couples underwent the basic evaluation consisting of history (age, BMI, duration and type of infertility, medical history, previous surgical procedures, and lifestyle), physical examination, and investigations to assess the etiology of infertility prior to the IUI procedure. These investigations included a female hormonal profile on day two of the menstrual cycle (FSH, LH, E2, TSH/T_4 and prolactin levels), measurement of mid-luteal serum progesterone and anti-mullerian hormone (AMH) level at any time of the cycle for participants 35 years and above, a baseline gynaecological scan, an office hysteroscopy if indicated, and semen analysis. Additionally, participants were screened for syphilis, HIV, hepatitis (B&C), and immunity to rubella. Fallopian tube patency was assessed by hysterosalpingography or laparoscopy with chromoperturbation.

Ovarian stimulation

Most female participants were treated with ovarian stimulation agents, either clomiphene citrate (CC) alone, Letrozole (Femara®) alone, gonadotrophin injections (Gonal-F®, Menopur®, Fostimon®) alone, or with a combination of CC/Letrozole and gonadotrophin. Serial transvaginal ultrasound was used to monitor ovarian response on cycle days 10 to 14, assessing follicular growth and endometrial thickness. Human Chorionic Gonadotrophin (Ovitrelle® 250 mcg) was administered if at least 1 follicle had a mean diameter ≥ 18 mm. IUI was performed 24–40 hours post-hCG (human chorionic gonadotropin) injection with a maximum of three dominant follicles. Luteal phase support with progesterone(Utrogestan®) supplementation was given in cases with known luteal phase defect.

Sperm preparation

The husband or partner was required to give semen on the same day of IUI. A prewash analysis in terms of volume, counts, motility, and forward progression was done. The sample was then processed and underwent a standard gradient wash. If the partner or husband was HIV-positive, the sample underwent a double wash. The post-wash sample parameters were assessed before the sample was put in a 14 ml conical test tube and kept in a warming block until the female was ready and prepped for insemination.

Intrauterine insemination

In most cycles, a single IUI was performed with a 1 ml syringe using a soft IUI catheter (Tomcat®, Gynetics™) or, alternatively, a rigid catheter. The patient in the lithotomy position and using the standard aseptic technique, a gentle insertion of the catheter through the cervical canal was followed by the injection of 0.5 ml sperm preparation into the uterine cavity. The bed was tilted electronically into the Trendelenburg position after which the catheter was withdrawn. The patient was then placed supine but still in Trendelenburg, and was left to lie for a further 10−15 minutes thereafter.

Pregnancy test

Two weeks after the IUI procedure, a serum quantitative pregnancy test was done. If the pregnancy test was positive, the test was repeated 48 hours later to ensure that the levels were increasing as expected. If levels remained low or declined and if a gestational sac was not visible on transvaginal ultrasound four weeks post-IUI, it was recorded as a biochemical pregnancy. If a gestational sac was noted on the transvaginal ultrasound, it was noted as a clinical pregnancy.

Statistical analysis

We used STATA Version 17 (Stata Corp) to analyse our data. Continuous variables were described with means (±SD) and medians (IQR) while categorical variables were expressed as frequencies and percentages. The independent t-test, Mann-Whitney U-test, and Pearson's Chi-Square or Fisher exact test were used to analyse association between continuous and categorical variables, respectively. Multivariate logistic regression was carried out to identify significant predictors of successful IUI. For all comparisons, a p-value of <0.05 was considered statistically significant.

RESULTS

Couple characteristics

We evaluated 273 couples who underwent intrauterine insemination from January 2019 to June 2021. Eleven couples (4%) were HIV affected, ten of which were discordant couples. There were six couples with an HIV-positive male partner and four couple an HIV-positive female partner.

Male characteristics

The mean male age was 37.15 years (SD±5.16). The majority had a PTMSC of more than 39 x 10^6/ml and a sperm motility greater than or equal to 70%. (Table 1)

Table 1: Male characteristics with pregnancy rate

Variables	Pregnancy Negative n(%)	Pregnancy Positive n(%)	Total
Male Age (years)			
< 40	144(75.8)	46(24.2)	190
≥ 40	70(84.3)	13(15.7)	83
PTMSC (/ml)			
< 4 x 10^6	0(0)	1(100)	1
≥ 4 - 15 x 10^6	27(84.4)	5(15.6)	32
> 15 - 39 x 10^6	62(92.5)	5(7.5)	67
> 39 -150 x 10^6	123(71.9)	48(28.1)	171
> 150 x 10^6	2(100)	0(0)	2
Sperm Motility (%)			
< 70	26(89.7)	3(10.3)	29
≥ 70	188(77)	56(23)	244
HIV status for Male			
Negative	208(78.2)	58(21.8)	266
Positive	6(85.7)	1(14.3)	7

Female characteristics

The mean female age was 33.51 years (SD±4.83), with most being in the age group 30−35 years. Twelve females (4.4%) were obese, and the majority did not have any other known comorbidities. Most of the females had primary infertility and the median duration of infertility was three years (IQR: 2-5). The main cause of infertility was ovulatory dysfunction, followed by unexplained infertility. (Table 2)

Table 2: Female characteristics with pregnancy rate

Variables	Pregnancy Negative n(%)	Pregnancy Positive n(%)	Total
Female Age (years)			
< 30	42(73.7)	15(26.3)	57
30 – 35	86(77.5)	25(22.5)	111
36 – 40	64(80)	16(20)	80
> 40	22(88)	3(12)	25
BMI			
Normal	178(77.7)	51(22.3)	229
Overweight	26(81.2)	6(18.8)	32
Obese	10(83.3)	2(16.7)	12
Duration of infertility (years)			
< 5	149(76)	47(24)	196
≥ 5	65(84.4)	12(15.6)	77
Type of infertility			
Primary	128(79.5)	33(20.5)	161
Secondary	86(76.8)	26(23.2)	112
Cause of infertility			
Male factor	34(77.3)	10(22.7)	44
Cervical factor	5(83.3)	1(16.7)	6
Unexplained	40(83.3)	8(16.7)	48
Endometriosis	12(80)	3(20)	15
Sexual disorders[a]	5(100)	0(0)	5
Ovulatory dysfunction	77(74.8)	26(25.2)	103
No partner	5(83.3)	1(16.7)	6
Combined	36 (78.3)	10(21.7)	46
Comorbidities			
None	194(78.9)	52(21.1)	246
HIV- positive	4(80)	1(20)	5
Hypertension	2(66.7)	1(33.3)	3
Diabetes mellitus	2(100)	0(0)	2
Autoimmune	5(83.3)	1(16.7)	6
Other[b]	7(63.6)	4(36.4)	11

[a]Erectile dysfunction
[b]other (hyperthyroidism, sarcoidosis, hypercholesterolemia, epilepsy and colitis)

Cycle characteristics

We evaluated 273 couples during a total of 451 IUI cycles. All couples had a minimum of one IUI cycle; 136 had two cycles and 42 had three cycles. The average number of IUI cycles each couple underwent was 1.97 (SD±0.76) (range 1–3). Letrozole was the main ovarian stimulation agent in all the cycles (86%). The mean number of dominant follicles were 1.63 (SD±0.69). The mean size of follicles per stimulated cycle was 18.64 mm (SD±1.43) at the time of the ovulation trigger, with ovulation being triggered in the majority of participants in all three cycles. The median endometrial thickness per stimulated cycle was 7.3 mm (IQR: 6.5-8.5) and

the majority of cycles did not receive luteal support in the form of progesterone supplementation. (Table 3 and 4)

Table 3: Cycle characteristics with pregnancy rate

Variables	Pregnancy Negative n(%)	Pregnancy Positive n(%)	Total
Stimulation regimen			
Natural	17(100)	0(0)	17
Clomiphene Citrate	20(76.9)	6(23.1)	26
Letrozole	341(87.7)	48(12.3)	389
FSH/HMG	2(100)	0(0)	2
Combined	12(70.6)	5(29.4)	17
Number of follicles			
1	196(89.1)	24(10.9)	220
2	152(86.4)	24(13.6)	176
3	44(80)	11(20)	55
Size of follicles (mm)			
< 18	102(92.7)	8(7.3)	110
≥18	290(85)	51(15)	341
Ovulation trigger			
No	25(96.2)	1(3.8)	26
Yes	367(86.4)	58(13.6)	425
Endometrial thickness (mm)			
<7	159(88.8)	20(11.2)	179
≥7	233(85.7)	39(14.3)	272
Luteal support			
Yes	24(82.8)	5(17.2)	29
No	368(87.2)	54(12.8)	422
Number of cycles			
1	234(85.7)	39(14.3)	273
2	121(89)	15(11)	136
3	37(88.1)	5(11.9)	42

IUI outcome

The pregnancy rate was 14.3% (39/273) in the first cycle, 11% (15/136) in the second cycle, and 11.9% (5/42) in the third cycle. The overall pregnancy rate per intrauterine insemination was 13.1% per cycle and a cumulative pregnancy rate of 21.6% per couple after three treatment attempts. We found that 95% of females who conceived were 40 years of age or less compared to 5% who were over 40 years (Table 4). Females who had a successful IUI with duration of infertility < 5 years and ≥ 5 years were 47 (24%) and 12 (15.6%), respectively. A higher pregnancy rate was observed in females with secondary infertility compared to females with primary infertility (14.5% vs 12.1%).

Table 4: Pregnancy rates per female stratification and cycle

Age	Number of females	Number of cycles	Number of pregnancies	Rate of pregnancy per female (%)	Rate of pregnancy per cycle (%)
< 30	57	89	15	5.5	3.3
30 - 35	111	182	25	9.1	5.5
36 - 40	80	139	16	5.9	3.6
> 40	25	41	3	1.1	0.7
Total	273	451	59	21.6	13.1

Our study has shown a higher pregnancy rate when the cause of infertility was ovulatory dysfunction in females (16.2%) and male factor in 13.5%. There were 59 pregnancies in total, of which 56 were clinical and three biochemical. There were two miscarriages and one multiple pregnancy, a triplet. The live birth rate per cycle was 11.9% (54/451) (Table 5).

In the univariate analysis, the female age (32.5 vs. 33.9 years, p-value = 0.0345) and the duration of infertility (p-value = 0.0319) were found to be significantly associated with the chance of success (Table 6). Furthermore, PTMSC and follicle size significantly increased the pregnancy rate (Tables 7 and 8).

Table 5: Pregnancy outcome of intrauterine insemination cycles

Variables	Outcome/cycle(%)
Pregnancies/cycle	59/451(13.1)
Biochemical pregnancies	3/451(0.7)
Live births	54/451(11.9)
Miscarriages	2/59(3.3)
Singleton pregnancies	53/59(89.8)
Multiple pregnancies	1/59(1.7)

Table 6: Parameters affecting the success of IUI

Variables	Pregnancy		p-value
	Yes	No	
Female age	32.5 ± 4.73	33.9 ± 4.74	0.0345§
Duration of infertility(IQR)	3(2-4)	3(2-5)	0.0319$

$: Mann-Whitney u-test, §: Independent t-test

Table 7: Parameters affecting the success of IUI with respect to male and female characteristics

Variables		Pregnancies per cycle	%	p-value
Male Age	<40	47/312	15	0.061†
	≥ 40	12/139	8.6	
Processed TMSC	<4x10^6	1/1	100	0.001‡
	≥4 – 15 x10^6	5/48	10.4	
	>15 – 39 x10^6	5/114	4.3	
	>39x10^6	48/284	16.9	
	≥150x10^6	0/4	0	
Sperm motility	<70%	3/42	7.1	0.336‡
	≥70%	56/409	13.6	
BMI	Normal	51/375	13.6	0.873‡
	Overweight	6/56	10.7	
	obese	2/20	10	
Type of infertility	Primary	33/272	12.1	0.461†
	secondary	26/179	14.5	
Cause of infertility	Male factor	10/74	13.5	0.912‡
	Cervical	1/12	8.3	
	Unexplained	8/81	9.8	
	Endometriosis	3/26	11.5	
	Sexual disorders	0/8	0	
	Ovulatory dysfunction	26/160	16.2	
	No partner	1/9	11.1	
	Combined	10/81	12.3	

‡: Fisher's exact test, †: Chi-square test

Table 8: Parameters affecting the success of IUI with respect to cycle characteristics

Variables		Pregnancies per cycle	%	p-value
Stimulation regimen	Natural	0/17	0	0.085‡
	Clomiphene	6/26	23	
	Letrozole	48/389	12.3	
	FSH/HMG	0/2	0	
	Combined	5/17	29.4	
Number of follicles	1	24/220	10.9	0.194†
	2	24/176	13.6	
	3	11/55	20	
Size of follicles	<18 mm	8/110	7.2	0.038†
	≥18 mm	51/341	14.9	
Ovulation trigger	No	1/26	3.8	0.229‡
	Yes	58/425	13.6	
Endometrial thickness	<7 mm	20/179	11.1	0.579†
	≥7 mm	39/272	14.3	
Luteal support	Yes	5/29	17.2	0.209†
	No	54/422	12.7	
Number of Cycles	1	39/273	14.3	0.637†
	2	15/136	11	
	3	5 /42	11.9	

‡: Fisher's exact test, †: Chi-square test

On multivariate logistic regression of successful IUIs, none of the parameters were found to significantly influence the pregnancy rate (Table 9). However, there were more pregnancies with male age less than 40 years, PTMSC above 39 x 10^6/ml, female age between 30 and 35 years, and duration of infertility of less than five years. Pregnancy rates also appeared to increase with a combined stimulation regimen, an increased number of dominant follicles, a dominant follicle size of more than 18 mm, and if a trigger injection was used. However, none of these were statistically significant.

Table 9: The multivariate logistic regression of predictive parameters for IUI

Variables	**OR**	**95%CI**	**p-value**
Male age stratification	0.56	0.27 – 1.17	0.126
PTMSC	1.42	0.90 – 2.23	0.133
Female age stratification	0.92	0.64 – 1.32	0.650
Duration of infertility	0.70	0.35 – 1.39	0.307
Stimulation regimen	1.54	0.91 – 2.60	0.106
Number of follicles	1.26	0.85 – 1.87	0.252
Size of follicles	1.96	0.89 – 4.33	0.096
Ovulation trigger	3.05	0.40 – 23.57	0.284

OR: odds ratio, C.I: Confidence interval

DISCUSSION

This study described couples who underwent IUI, looking at various male and female parameters, parameters related to the ovarian stimulation process and the procedure itself, and the effect of these parameters on the success rate of IUI.

In our study, there was a higher pregnancy rate per cycle in males age less than 40 (15% vs 8.6%) regardless of female age. Contrary an earlier study has shown male age to be important when the female age is more than 35 years, but no difference was observed if the female was less than 35 years of age [9].

The majority (62.6%) of males in this study had a PTMSC > 39 x 10^6/ ml, which had a significant effect on the pregnancy rate per cycle (p-value = 0.001). Studies have reported that the PTMSC at a threshold of > 1 x 10^6/ml is associated with an increased pregnancy rate [10, 11]. A study has demonstrated that sperm motility > 50% was significantly associated with an increased pregnancy rate [12]. Present results showed that 89% of males had a sperm motility ≥ 70% with 13.6% (56/409) pregnancy rate.

Our study has also shown that female age was significantly associated with the pregnancy rate (32.5 vs 33.9 years, p-value = 0.0345), with a trend toward a decrease in success rate with OI-IUI being noted in females aged over 40 years. Several studies have also reported a significant decrease in the success rate beyond the age of 40 years, with documented live births being as low as 1.4% [13].

In our present study, there was no statistical significance between BMI and pregnancy rate; and this corresponds with a similar finding of a precedent study [14].

We also found that the pregnancy rate was significantly lower in association with an increase in the duration of infertility in female participants (p-value = 0.0319). A similar finding was documented in a study which suggested that IUI should not be recommended for patients with a long-standing history of infertility [15].

Despite the fact that the type of infertility had no statistically significant impact on the success rate in our study, a related study has shown that women with secondary infertility had a higher chance of becoming pregnant than those with primary infertility [15]. In terms of IUI indications, we discovered that ovulatory dysfunction 16.2% (26/160) and male factor 13.5%(10/74) had higher success rates compared to unexplained infertility 9.8% (8/81) and other causes, but the difference was not statistically significant. Ovulatory dysfunction and male factors were associated with the highest clinical pregnancy rates, according to numerous studies [16]. However, contrary to other causes, it was discovered in other studies that unexplained infertility had a higher likelihood of clinical pregnancy [17].

In our study, in most cycles (86.2%) Letrozole (Femara®) was used as the drug of choice for ovarian stimulation, with a pregnancy rate of 12.3% per cycle. Khalil et al. found that the probabilities of getting pregnant with IUI using ovarian stimulation were double compared with IUI alone [18]. Furthermore, most studies have shown that the pregnancy rates with FSH/HMG were higher compared to those where CC or letrozole was used [19].

With respect to the number of dominant follicles, our study found no statistical difference in the success rate for one dominant follicle compared to two or three. In contrast to our study, many studies reported an IUI success rate of 2−3 times higher with three dominant follicles than with one [20, 21], the difference is probably due to the small size of our sample. Our study also found a significantly higher pregnancy rate when the dominant follicle size was ≥ 18 mm compared to < 18 mm (p-value=0.038). Equivalent results were reported by Fallah

Tafti et al., who showed a higher pregnancy rate in patients with a dominant follicle ≥ 20 mm in size compared with those with a dominant follicle of < 20 mm [22].

In infertile couples undergoing OI-IUI, hCG trigger is associated with an increased pregnancy rate compared with spontaneous serum LH surge [23]. In our study, there was a higher pregnancy rate in IUI cycles when the hCG trigger was administered compared to the IUI cycle when hCG trigger was not given, though the difference was not significant.

Regarding endometrial thickness, we found a trend towards an increase in pregnancy rate with endometrial thickness ≥ 7 mm compared to < 7 mm. Esmailzadeh et al. showed that the endometrial thickness on the day of hCG administration was significantly greater in cycles where pregnancy was achieved [24]. In addition, Reuter et al. have shown that an endometrial thickness of at least 8 mm correlated with a higher pregnancy rate [25].

With respect to luteal support, our study found that the majority of females (93.6%) did not need luteal support. Ninety-two percent of cycles were induced with CC and Letrozole, with 12.7% (54/422) of pregnancies not receiving additional luteal support. According to Green et al.'s meta-analysis, exogenous progesterone during the luteal phase improves both clinical pregnancy and live birth rates in patients undergoing gonadotropin OI-IUI. This does not apply to CC/Letrozole ovulation induction cycles due to physiological differences in luteal function after ovulation induction with gonadotropins compared with CC or Letrozole [26].

In our study, couples received a maximum of three IUI cycles with the pregnancy rate being highest in the first cycle (14.3%) compared to the two other cycles, where it remained around 11.0%, although the difference was not statistically significant. This is in agreement with the study of Tomlinson et al. which reported a slow decrease in pregnancy rate per cycle for the first (22.3%), second (18.0%), and third (14.0%) cycles [27].

Predictive factors for pregnancy

We also attempted to discover which parameters were predictive for pregnancy after intrauterine insemination. For this purpose, logistic regression analysis was carried out and eight predictive parameters were selected in the univariate logistic regression: male age, PTMSC, female age, duration of infertility, stimulation regimen, number of follicles, size of follicle and ovulation trigger. In the multivariate logistic regression, none of the parameters were however found to be statistically predictive of the pregnancy rate. Several studies have reported female age as a significant predictor of successful IUI where advancing female age reduced female fertility due to decreased oocyte quality and quantity [28]. Tomlinson et al.

found PTMSC, duration of infertility, and number of follicles among the predictors [27]. A study by Khalil et al. also found the stimulation regimen to be a significant predictor of successful IUI [18]. According to Fallah Tafti et al., an optimal follicle size is important in terms of the pregnancy success rate in an ovarian stimulated IUI cycle [22].

Limitations of the study

The study is limited in that it is a retrospective design and has a small sample size. Moreover, we did not assess the cycle cancellation rate. Another limitation is the very small number of participants who received gonadotropins(FSH/HMG) as an ovarian induction agent, resulting in insufficient data to form conclusions regarding the use of luteal phase progesterone support.

Strengths of the study

Despite the limitations, our study provides useful findings. Significant pregnancy rates with increased PTMSC, younger female age, shorter duration of infertility, and follicle size ≥ 18 mm. Younger male age, stimulation regimen incorporating gonadotrophins, increased number of follicles, and use of an ovulation trigger injection were also found to be important parameters associated with successful IUI. These findings will help to better counsel couples with infertility undergoing ART in the form of IUI, with regard to various parameters which are likely to influence their success of achieving pregnancy through IUI.

CONCLUSIONS

Summary of main findings

IUI is an effective choice of therapy for infertility in a selected couple as first line ART. In our study, the overall pregnancy rate per cycle and the live birth rate per cycle were 13.1% and 11.9%, respectively. The cumulative pregnancy rate over three IUI cycles was 21.6%. Favourable parameters for treatment success were PTMSC > 39 x 10^6/ml, female age less than 40 years, duration of infertility less than five years, and follicle size ≥ 18 mm at the time of ovulation trigger injection. Most pregnancies occur during the first cycle. Other parameters such as male age, stimulation regimen, and number of follicles did not have a significant effect on the IUI success rate.

Recommendations

Additional studies with a larger series of couples are needed to confirm the beneficial findings in this study.

Data availability

Data supporting the conclusions of this article will be shared upon reasonable request to the corresponding author.

Conflicts of interest
None

Funding
None

Acknowledgements
We wish to express our gratitude to Ms SB Kagodora, who assisted with statistical analysis.

Authors contribution
All authors participated in the elaboration of the study.

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APPENDIX A: Ethics clearance

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Mulema Noel Feti

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M211017

NAME: (Principal Investigator)	Dr Mulema Noel Feti
DEPARTMENT:	Obstetrics and Gynaecology BioART Fertility Centre
PROJECT TITLE:	An evaluation of couples undergoing intrauterine insemination in a clinic in Johannesburg
DATE CONSIDERED:	29/10/2021
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Y. Adam and Dr T. Mohamed
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	02/11/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I **agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **October** and will therefore be due in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

03/11/2021
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX B: Permission to conduct research from BioArt

BioART.
Fertility Centre

99 Oxford Road
Saxonwold, 2196
Tel: + 27 11 484 5119 • + 27 11 484 5168
Postal Address: P. O. Box 2590, Houghton 2041
reception@bioartfertility.co.za
adila@bioartfertility.co.za
www.bioartfertility.co.za

19 July 2021

To whom it may concern,

This letter serves to confirm that Dr Tasneem Mohamed of the BioART fertility centre will be co-supervising the MMed of Dr Noel Fetty of the University of the Witwatersrand.

Dr Fetty's research involves the evaluation of various parameters which affect the likelihood of successful conception with Intrauterine Insemination.

This study will be done retrospectively and will require the analysis of the data of patients that have undergone this treatment.

The doctors at BioART namely, Dr Mohamed, Dr Cassim and Dr Dasoo will allow Dr Fetty access to our patient's information. Only the necessary information will be collected and analysed. Collected Data will be transferred to a data collection sheet.
We stress upon the strict anonymity of our patients in accordance with the POPI Act No. 4 of 2013. As such, all study files will be allocated a study number and no identifiable information will be revealed.

Should you have any queries please do not hesitate to contact us.

Regards,

Dr Tasneem Mohamed

Dr Mohamed Iqbal Cassim

Dr Yusuf Dasoo

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