

https://dspace.org/

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

Feti, Mulema Noel

2024
University of the Witwatersrand, Johannesburg
https://hdl.handle.net/10539/46573

Feti, Mulema Noel. (2024). An Evaluation of Couples Undergoing Intrauterine Insemination in a Clinic in Johannesburg [Master`s dissertation, University of the Witwatersrand, Johannesburg]. WIReDSpace. https://hdl.handle.net/10539/46573

Downloaded from a DSpace repository. https://dspace.org/

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)

by

Dr Mulema Noel FETI

Student no**:** 2535102

MMed **(**Obstetrics and Gynaecology)

Supervisors

Prof. Y Adam: BSc, MBChB, FCOG(SA)

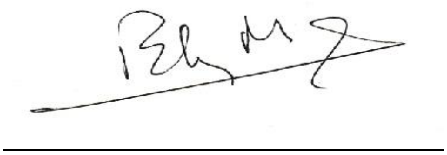
Dr T Mohamed: MBChB (Wits), FCOG(SA), MMed(O&G) (Wits)

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

ACKNOWLEDGEMENTS

First of all, I would like to thank my Lord Jesus Christ for His grace upon me to carry out this study.

Secondly, I would like to express my sincere gratitude to my supervisors Professor Y. Adam and Dr T. Mohamed for providing their invaluable guidance throughout the course of the project.

Thirdly, I wish to express my gratitude to Ms SB Kagodora, who assisted with statistical analysis.

Finally, I would like to thank my wife Nathalie and my children Chris-Noel and Charis-Anne, for their continuous support and understanding when undertaking this project.

PRESENTATION ARISING FROM THIS PROJECT

Poster Presentation:

Abstract submitted and accepted for poster presentation at International Federation of fertility societies World Congress: 10-13 September 2023.

TABLE OF CONTENTS

DECLARATION ii
ACKNOWLEDGEMENTS iii
PRESENTATION ARISING FROM THIS PROJECT iv
LIST OF TABLES vi
ABBREVIATIONS vii
ARTICLE viii
ABSTRACT 1
INTRODUCTION 2
MATERIALS AND METHODS 3
Participants 3
Ovarian stimulation 3
Sperm preparation 4
Intrauterine insemination 4
Pregnancy test 4
Statistical analysis 4
RESULTS 5
Couple characteristics 5
Male characteristics 5
Female characteristics 5
Cycle characteristics 6
IUI outcome 7
DISCUSSION 10
Predictive factors for pregnancy 12
Limitations of the study 13
Strengths of the study 13
CONCLUSIONS 13
Summary of main findings 13
Recommendations 13
Data availability 13
Conflicts of interest 14
Funding 14
Acknowledgements 14
Authors contribution 14
REFERENCES 14

APPENDIX A: Ethics clearance 17
APPENDIX B: Permission to conduct research from BioArt 18
APPENDIX C: Author guidelines 19
APPENDIX D: Plagiarism declaration form 30

LIST OF TABLES

Table 1: Male characteristics with pregnancy rate 5

Table 2: Female characteristics with pregnancy rate 6

Table 3: Cycle characteristics with pregnancy rate 7

Table 4: Pregnancy rates per female stratification and cycle 8

Table 5: Pregnancy outcome of intrauterine insemination cycles 8

Table 6: Parameters affecting the success of IUI 8

Table 7: Parameters affecting the success of IUI with respect to male and female characteristics 9

Table 8: Parameters affecting the success of IUI with respect to cycle characteristics 9

Table 9: The multivariate logistic regression of predictive parameters for IUI 10

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

***Feti MN,** MBChB;[1] **Adam Y**, BSc, MBChB, FCOG(SA);[1] **Mohamed T,** MBChB, FCOG (SA)[2]

[1]*Department of Obstetrics and Gynaecology, School of Medicine, University of the Witwatersrand, Johannesburg, South Africa*

[2] *BioArt Fertility Centre, Johannesburg, South Africa*

***Corresponding author: Mulema Noel Feti (2535102@students.wits.ac.za; noelfety@gmail.com)**

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.

REFERENCES

1. World Health Organization (WHO). International classification of diseases, 11th revision (ICD-11) Geneva: WHO; 2018.

2. Practice Committee of American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: A committee opinion. Fertil Steril 2013; 99:63. doi: 10.1016/j.fertnstert.2012.09.023

3. Rutsein SO, Shah IH, Infecundity, infertility, and childlessness in developing countries. Geneva: World Health Organization; 2004.

4. Forti G, Krausz C. Evaluation and treatment of the infertile couple. J Clin Endocrinol Metab December 1998; 83(12): 4177–88. doi: 10.1210/jcem.83.12.5296

5. Cohlen B, Ombelet W (Eds). Intra-uterine insemination: Evidence-based guidelines for daily Practice; London, CRC Press: 2013. doi: 10.1201/9780367808082

6. Soria M, Pradillo G, García J, et al. Pregnancy predictors after intrauterine insemination: Analysis of 3012 cycles in 1201 couples. J Reprod Infertil. 2012; 13(3): 158–66

7. Adamson GD, Baker VL. Sub fertility: Causes, treatment and outcome. Best Pract Res Clin Obst Gynecol 2003; 17(2): 169-85. doi: 10.1016/s1521-6934(02)00146-3

8. Guzick DS, Carson SA, Coutifaris C, et al. Efficacy of superovulation and intrauterine insemination in the treatment of infertility. National Cooperative Reproductive Medicine Network. N Engl J Med. 1999; 340:177-83. doi:10.1056/NEJM199901213400302

9. Brzechffa PR, Buyalos RP. Female and male partner age and menotrophin requirements influence pregnancy rates with human menopausal gonadotrophin therapy in combination with intrauterine insemination. Hum Reprod 1997; 12(1):29–33. doi: 10.1093/humrep/12.1.29

10. Ombelet W, Vandeput H, Vande Putte G, et al. Intrauterine insemination after ovarian stimulation with clomiphene citrate: Predictive potential of inseminating motile count and sperm morphology. Hum Reprod 1997; 12:1458–63. doi: 10.1093/humrep/12.7.1458

11. Merviel P, Heraud MH, Grenier N, et al. Predictive factors for pregnancy after intrauterine insemination (IUI): An analysis of 1038 cycles and a review of the literature. Fertil Steril. 2010; 93:79–88. doi: 10.1016/j.fertnstert.2008.09.058

12. Yavuz A, Demirci O, Sözen H, et al. Predictive factors influencing pregnancy rates after intrauterine insemination. Iran J Reprod Med. 2013;11(3):227-34.

13. Frederick JL, Denker MS, Rojas A, et al. Infertility: Is there a role for ovarian stimulation and intra-uterine insemination after age 40? Hum Reprod 1994 Dec;9(12):2284-6. doi: 10.1093/oxfordjournals.humrep.a138438

14. Souter I, Baltagi LM, Kuleta D, et al. Women, weight, and fertility: The effect of body mass index on the outcome of superovulation/ intrauterine insemination cycles. Fertil Steril. 2011; 95:1042–7. doi: 10.1016/j.fertnstert.2010.11.062

15. Zadehmodarres S, Oladi B, Saeedi S, et al. Intrauterine insemination with husband semen: An evaluation of pregnancy rate and factors affecting outcome. J Assist Reprod Genet. 2009;26(1):7-11. doi: 10.1007/s10815-008-9273-7

16. Costello MF. Systematic review of the treatment of ovulatory infertility with clomiphene citrate and intrauterine insemination. Aust N Z J Obstet Gynaecol 2004; 44:93-102. doi: 10.1111/j.1479-828X.2004. 00192.x

17. Ahinko K. Successful Intrauterine Insemination Treatment. Finland: University of Tempere; 2009: 24-5.

18. Khalil MR, Rasmussens PE, Erb K, et al. Homologous intrauterine insemination: An evaluation of prognostic factors based on a review of 2473 cycles. Acta Obstet Gynaecol Scand 2001; 80: 74-81. doi: 10.1034/j.1600-0412.2001. 800115.x

19. Cantineau AEP, Cohlen BJ. Ovarian stimulation protocols (anti-oestrogens, gonadotrophins with and without GnRH agonists/antagonists) for intrauterine insemination (IUI) in women with subfertility. Cochrane Database Syst Rev. 2007;(2):CD005356. doi: 10.1002/14651858.CD005356

20. Nuojua-Huttunen S, Tomas C, Bloigu R, et al. Intrauterine insemination treatment in subfertility: an analysis of factors affecting outcome. Hum Reprod 1999; 14: 698-703. doi: 10.1093/humrep/14.3.698

21. Dickey RP, Taylor SN, Lu PY, et al. Effect of diagnosis, age, sperm quality, and number of preovulatory follicles on the outcome of multiple cycles of clomiphene citrate-intrauterine insemination. Fertil Steril 2002; 78: 1088-95. doi: 10.1016 /s0015-0282(02)04212-7

22. Fallah Tafti T, Yasaei M, Dehghani-Firouzabadi R, et al. Evaluation of the appropriate size of follicles on success rate in patient undergoing controlled ovarian stimulation and intrauterine insemination cycles. J adv med sci appl technol. 2017; 3(2); 101-8. doi: 10.18869/nrip.jamsat.3.2.101

23. Taerk E, Hughes E, Greenberg C, et al. Controlled Ovarian Hyperstimulation with Intrauterine Insemination Is More Successful After r-hCG Administration Than Spontaneous LH Surge. J Reprod Infertil. 2017 Jul-Sep;18(3):316-322. PMID: 29062796; PMCID: PMC5641441.

24. Esmailzadeh S, Faramarzi M. Endometrial thickness and pregnancy outcome after intrauterine insemination. Fertil Steril 2007; 88: 432-7. doi: 10.1016/j.fertnstert.2006.12.010

25. Reuter H, Cohen S, Fureg C, et al. sonographic appearance of the endometrium and ovaries during cycles stimulated with human menopausal gonadotropin. J Reprod Med. 1996; 41:509-14.

26. Green KA, Zolton JR, Schermerhorn SM et al. Progesterone luteal support after ovulation induction and intrauterine insemination: An updated systematic review and meta-analysis. Fertil Steril. 2017;107(4):924-33. doi: 10.1016/j.fertnstert.2017.01.011

27. Tomlinson MJ, Amissah-Arthur JB, Thompson KA, et al. Prognostic indicators for intrauterine insemination (IUI): Statistical model for IUI success. Hum Reprod. 1996 Sep;11(9):1892-6. doi: 10.1093/oxfordjournals.humrep.a019513

28. Zippl AL, Wachter A, Rockenschaub P, et al. Predicting success of intrauterine insemination using a clinically based scoring system. Arch Gynecol Obstet 2022 Nov;306(5):1777-86. doi: 10.1007/s00404-022-06758-z

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

BioART
Reg No. 2005/015157/23
P O BOX 2590, HOUGHTON 2041
Tel. (011) 484-5119 (011) 647-9110
Fax: (011) 484-5180

Dr. M.I. Cassim
MBBCh (Wits) F.C.O.G (SA)
Mphil (Repro) Stellenbosch
Dip B.A. (Edinburgh)
MBA (Edinburgh),

Practice No. **0204153**

Dr. Y.M. Dasoo
MBBCh (Wits) F.C.O.G (SA)
MSC (Repro Physiology)
Stellenbosch

APPENDIX C: Author guidelines

Author guidelines for International Journal of Reproductive Medicine

Publish with Hindawi:

Join our community of authors and benefit from:

- An easy-to-use manuscript submission system, without manuscript formatting requirements.
- Free of charge, full language editing report at point of submission, to help you assess and improve your manuscript prior to peer review.
- Dedicated editors who are active in their specific communities.
- High editorial standards, ensuring all published manuscripts undergo an in-depth peer review process.
- Quick, efficient publication with full transparency on all publishing metrics and turnaround times.
- Greater impact, reach, and visibility of your research through open access.
- Retention of all ownership and copyright of your published research.
- Discount on a wide range of author services from leading providers, to help make your manuscript the best it can be.

Language editing and author services

We have partnered with a number of leading author services providers to offer our authors an exclusive 10% discount on a wide range of manuscript preparation and post-publication services. This discount applies to various language editing, translation, and research communication services. Learn more about author services.

You can make use of a free artificial intelligence (AI)-based language editing tool, Writefull, at the point of submission. Writefull will scan your manuscript and make suggestions to help improve the quality of your writing. The tool applies machine learning, trained on millions of published scientific articles, and suggests improvements to grammar, spelling, and academic language.

Submission

Manuscripts should be submitted by one of the authors of the manuscript through Phenom, the manuscript submission system for our journals. Only electronic PDF (.pdf) or Word (.doc, .docx, .odt, .rtf, .txt) files can be submitted through the manuscript submission system, and there is no page limit. Special characters should not be included in the file name of the main manuscript file. Submissions by anyone other than one of the authors will not be accepted. The submitting author takes responsibility for the manuscript during submission and peer review. For technical help, please contact help@hindawi.com.

Terms of submission

Manuscripts must be submitted on the understanding that they have not been published elsewhere and are only being considered by this journal. The submitting author is responsible for ensuring that the article's publication has been approved by all the other co-authors. It is also the submitting author's responsibility to ensure that the article has all necessary institutional approvals. Only an acknowledgment from the editorial office officially establishes the date of receipt. Further correspondence and proofs will be sent to the author(s) before publication, unless otherwise indicated. It is a condition of submission that the authors permit editing of the manuscript for readability. All inquiries concerning the publication of accepted manuscripts should be addressed to help@hindawi.com. All submissions are bound by Hindawi's terms of service.

Peer review

All submitted articles are subject to assessment and peer review to ensure editorial appropriateness and technical correctness.

Research published in the journal must be:

- Scientifically valid – adhering to accepted community standards of research.
- Technically accurate in its methods and results.
- Representative of a specific advance, or replication, or null/negative result, which is worthy of publication.
- As reproducible as possible – sharing underlying data, code, and supporting materials wherever able.
- Ethically sound and transparent — adhering to best practice with respect to animal and human studies, consent to publish, and clear declaration of potential conflicts of interests, both real and perceived.

In the spirit of sharing findings through our open science mission, emphasis is not placed on novelty, interest, or perceived impact. Replication studies, particularly of research published in this journal, are encouraged.

In order for an article to be accepted for publication, the assigned editor will first consider if the manuscript meets the minimum editorial standards and fits within the scope of the journal. If an article is considered suitable for the journal, the editor will ideally solicit at least two external peer reviewers (who will remain anonymous to the authors unless they choose to disclose their identity by signing the review report) to assess the article before confirming a decision to accept. Decisions to reject are at the discretion of the editor.

Our research integrity team will occasionally seek advice outside standard peer review, for example, on submissions with serious ethical, security, biosecurity, or societal implications. We may consult experts and the editor before deciding on appropriate actions, including but not limited to: recruiting reviewers with specific expertise, assessment by additional editors, and declining to further consider a submission.

Concurrent submissions

In order to ensure sufficient diversity within the authorship of the journal, authors will be limited to having three manuscripts under review at any point in time. If an author already has three manuscripts under review in the journal, they will need to wait until the review process of at least one of these manuscripts is complete before submitting another manuscript for consideration. This policy does not apply to editorials or other non-peer-reviewed manuscript types.

Article processing charges

The journal is open access. Article processing charges (APCs) allow the publisher to make articles immediately available online to anyone to read and reuse upon publication.

Preprints

Hindawi supports the deposition of manuscripts in preprint servers, and does not consider this to compromise the novelty of the results. Articles based on content previously made public only on a preprint server, institutional repository, or in a thesis will be considered. The preprint should be cited.

Preregistration of studies

Authors are encouraged to indicate whether the conducted research was preregistered in an independent, institutional registry (e.g., http://clinicaltrials.gov/, https://www.socialscienceregistry.org/, http://osf.io/, https://egap.org/registry/, http://ridie.3ieimpact.org/). Preregistration of studies involves registering the study design, variables, and treatment conditions prior to conducting the research.

Preregistration of analysis plans

Authors are encouraged to indicate whether or not the conducted research was preregistered with an analysis plan in an independent, institutional registry (e.g., http://clinicaltrials.gov/, https://www.socialscienceregistry.org/, http://osf.io/, https://egap.org/registry/, http://ridie.3ieimpact.org/). Preregistration of studies involves registering the study design, variables, and treatment conditions. Including an analysis plan involves specification of sequence of analyses or the statistical model that will be reported.

ORCID

Prior to publication, an ORCID iD must be provided for the corresponding author(s). If you already have an ORCID iD, you will be asked to provide it. If you haven't registered with ORCID yet, we'll help you create an iD at the point of submission. The ORCID is not required for submission, or for peer review, but we will not be able to publish your article online until an ORCID iD is provided.

Article types

The journal will consider the following article types:

Research articles

Research articles should present the results of an original research study. These manuscripts should describe how the research project was conducted and provide a thorough analysis of the results of the project. Systematic reviews may be submitted as research articles.

Reviews

A review article provides an overview of the published literature in a particular subject area.

Formatting

An optional research article manuscript template can be downloaded here. We recommend that all manuscripts include line numbers and follow the structure below:

Title and authorship information

The following information should be included:

- Manuscript title
- Full author names
- Full institutional mailing addresses
- Email addresses

Affiliations. Hindawi Limited remains neutral with regard to jurisdictional claims in institutional affiliations. Responsibility for affiliations ultimately rests with the author, although Hindawi may request changes be made to countries listed in affiliations to ensure consistency across published output (for indexing and discovery reasons).

Abstract

The manuscript should contain an abstract. The abstract should be self-contained, citation-free, and should not exceed 300 words.

Introduction

This section should be succinct, with no subheadings.

Materials and methods

The methods section should provide enough detail for others to be able to replicate the study. If you have more than one method, use subsections with relevant headings, e.g. different models, in vitro and in vivo studies, statistics, materials and reagents, etc.

Hindawi journals have no space restriction on methods. Detailed descriptions of the methods (including protocols or project descriptions) and algorithms may also be uploaded as supplementary information or a previous publication that gives more details may be cited. If the method from a previous article is used then this article must be cited and discussed. If wording is reused from a published article then this must be noted, e.g. This study uses the method of Smith et al. and the methods description partly reproduces their wording [1].

If a method or tool is introduced in the study, including software, questionnaires, and scales, the license this is available under and any requirement for permission for use should be stated. If an existing method or tool is used in the research, the authors are responsible for checking the license and obtaining any necessary permission. If permission was required, a statement confirming permission was granted should be included in the materials and methods section.

Publishing protocols. We encourage authors describing any methodology, in particular laboratory-based experiments in the life sciences but also computational and bioinformatics protocols, to upload details of their methods to protocols.io. This is an open access website that allows researchers to record their methods in a structured way, obtain a DOI to allow easy citation of the protocol, collaborate with selected colleagues, share their protocol privately for journal peer review, and choose to make it publicly available. Once published, the protocol can be updated and cited in other articles.

You can make your protocol public before publication of your article if you choose, which will not harm the peer review process of your article and may allow you to get comments about your methods to adapt or improve them before you submit your article (see also the protocols.io FAQ page).

Results and discussion

This section may be divided into subsections or may be combined.

Main text (review only)

This section may be divided into subsections or may be combined.

Conclusions

This should clearly explain the main conclusions of the article, highlighting its importance and relevance.

Data availability

This statement should describe how readers can access the data supporting the conclusions of the study and clearly outline the reasons why unavailable data cannot be released.

Conflicts of interest

Authors must declare all relevant interests that could be perceived as conflicting. Authors should explain why each interest may represent a conflict. If no conflicts exist, the authors should state this. Submitting authors are responsible for coauthors declaring their interests.

Conflicts of interest (COIs, also known as 'competing interests') occur when issues outside research could be reasonably perceived to affect the neutrality or objectivity of the work or its assessment. For more information, see our publication ethics policy. Authors must declare all potential interests – whether or not they actually had an influence – in the conflicts of interest section, which should explain why the interest may be a conflict. If there are none, the authors should state: "The author(s) declare(s) that there is no conflict of interest regarding the publication of this article". Submitting authors are responsible for coauthors declaring their interests. Declared conflicts of interest will be considered by the editor and reviewers, and included in the published article.

Authors must declare current or recent funding (including for article processing charges) and other payments, goods or services that might influence the work. All funding, whether a conflict or not, must be declared in the funding statement. The involvement of anyone other than the authors who: i) has an interest in the outcome of the work; ii) is affiliated to an organization with such an interest; or iii) was employed or paid by a funder, in the commissioning, conception, planning, design, conduct, or analysis of the work, the preparation or editing of the manuscript, or the decision to publish must be declared.

You may be asked to make certain changes to your manuscript as a result of your declaration. These requests are not an accusation of impropriety. The editor or reviewer is helping you to protect your work against potential criticisms.

If you are in any doubt about declaring a potential conflict, remember that if it is revealed later – especially after publication – it could cause more problems than simply declaring it at the time of submission. Undeclared conflicts of interest could lead to a corrigendum or, in the most serious cases, a retraction.

Funding statement

Authors must state how the research and publication of their article was funded, by naming financially supporting body(s) (written out in full) followed by associated grant number(s) in square brackets (if applicable), for example: “This work was supported by the Engineering and Physical Sciences Research Council [grant numbers xxxx, yyyy]; the National Science Foundation [grant number zzzz]; and a Leverhulme Trust Research Project Grant”.

If the research did not receive specific funding, but was performed as part of the employment of the authors, please name this employer. If the funder was involved in the manuscript writing, editing, approval, or decision to publish, please declare this.

Acknowledgments

All acknowledgments (if any) should be included at the very end of the manuscript before the references. Anyone who made a contribution to the research or manuscript, but who is not a listed author, should be acknowledged (with their permission).

References

Authors may submit their references in any style. If accepted, these will be reformatted in Chicago style by Hindawi. Authors are responsible for ensuring that the information in each reference is complete and accurate. All references should be numbered consecutively in the order of their first citation. Citations of references in the text should be identified using numbers in square brackets e.g., “as discussed by Smith [9]”; “as discussed elsewhere [9, 10]”. All references should be cited within the text and uncited references will be removed.

Citation standards. All data, program code, and other methods should be appropriately cited. Such materials should be recognized as original intellectual contributions and afforded recognition through citation.

Date formatting

Hindawi recommends writing dates out fully to avoid confusion with different all-numeral date styles. For example, 11/10/2018 could be 10 November 2018 or 11 October 2018 depending on the reader, therefore, the date should be written out in full. For example, the date September 1, 2018 should be used rather than 01/09/2018 or 09/01/2018.

Units of measurement

Units of measurement should be presented simply and concisely using the International System of Units (SI).

Preparation of figures

Upon submission of an article, authors should include all figures and tables in the PDF file of the manuscript. Figures and tables should not be submitted in separate files. If the article is accepted, authors will be asked to provide the source files of the figures. Each figure should be supplied in a separate electronic file. All figures should be cited in the manuscript in a consecutive order. Figures should be supplied in either vector art formats (Illustrator, EPS, WMF, FreeHand, CorelDraw, PowerPoint, Excel, etc.) or bitmap formats (Photoshop, TIFF, GIF, JPEG, etc.). Bitmap images should be of 300 dpi resolution at least unless the resolution is intentionally set to a lower level for scientific reasons. If a bitmap image has labels, the image and labels should be embedded in separate layers.

Maps. Hindawi Limited remains neutral with regard to jurisdictional claims in published maps. For reasons of consistency, authors are requested to use accepted standard maps as the basis for map figure drawing, for example using the latest standard base-map of Map Press. Responsibility for maps rests with the author and it is their responsibility to also provide any copyright or licence information when using maps that are not owned or created by the author (e.g. Google Maps, etc.)

Preparation of tables

Tables should be cited consecutively in the text. Every table must have a descriptive title and if numerical measurements are given, the units should be included in the column heading. Vertical rules should not be used.

Supplementary materials

Supplementary materials are the additional parts to a manuscript, such as audio files, video clips, or datasets that might be of interest to readers. Authors can submit one file of supplementary material along with their manuscript through the manuscript submission system. If there is more than one file, they can be uploaded as a .ZIP file.

A section titled supplementary material should be included before the references list with a concise description for each supplementary material file. Supplementary materials are not modified by our production team. Authors are responsible for providing the final supplementary material files that will be published along with the article.

Proofs

Corrected proofs must be returned to the publisher within two to three days of receipt. The publisher will do everything possible to ensure prompt publication.

Copyright and permissions

Authors retain the copyright of their manuscripts, and all open access articles are distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided that the original work is properly cited.

The use of general descriptive names, trade names, trademarks, and so forth in this publication, even if not specifically identified, does not imply that these names are not protected by the relevant laws and regulations. The submitting author is responsible for securing any permissions needed for the reuse of copyrighted materials included in the manuscript.

While the advice and information in this journal are believed to be true and accurate on the date of its going to press, neither the authors, the editors, nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Reporting guidelines

Authors are strongly encouraged to use appropriate reporting guidelines when preparing and submitting manuscripts, to maximize transparency and reproducibility. Our editors and reviewers are also encouraged to use them in the review process. Completed checklists should be provided in the supplementary files on submission. We particularly encourage the use of:

- CONSORT for randomized controlled trials
- TREND for non-randomized trials
- PRISMA for systematic review and meta-analyses
- CARE for case reports
- STROBE for observational studies
- STREGA for genetic association studies
- SRQR for qualitative studies

- STARD for diagnostic accuracy studies
- ARRIVE for animal experiments

Ethical guidelines

In any studies on human or animal subjects, the following ethical guidelines must be observed. For any experiments on humans, all work must be conducted in accordance with the Declaration of Helsinki (1964). Manuscripts describing experimental work that carries a risk of harm to human subjects must include a statement that the experiment was conducted with the human subjects' understanding and consent, as well as a statement that the responsible ethics committee has approved the experiments. In the case of any animal experiments, the authors must provide a full description of any anaesthetic or surgical procedure used, as well as evidence that all possible steps were taken to avoid animal suffering at each stage of the experiment.

Appeals

Authors may appeal if they feel that the decision to reject was based on: i) a major misunderstanding over a technical aspect of the manuscript; or ii) a failure to understand the scientific advance shown by the manuscript. Appeals requesting a second opinion without sufficient justification will not be considered. To lodge an appeal, please contact the journal by email, quoting your manuscript number. Appeals will only be considered from the original submitting author.

APPENDIX D: Plagiarism declaration form

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Dr **Mulema Noel FETI (**Student number: 2535102) am a student registered for the degree of **MMed** (Obstetrics and Gynaecology) in the academic year 2021.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.

- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.

- I have followed the required conventions in referencing the thoughts and ideas of others.

- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: 

Date: 01/02/2023