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Original Research Article

## Single embryo transfer and multifetal pregnancy reduction: perception and attitude of women seeking assisted reproduction in Nigeria

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### ABSTRACT

**Background:** In-vitro fertilization (IVF) is associated with increased multiple pregnancy and its attendant complications. This study evaluates the attitude and acceptance of single embryo transfer (SET) and multifetal pregnancy reduction (MFPR) by clients assessing assisted reproduction in this region.

**Methods:** A cross sectional survey of patients selected for IVF was conducted. Information on demography, knowledge of IVF procedure and their perception, attitude and acceptability of multiple pregnancy as well as their knowledge, attitude and perception to single embryo transfer and multifetal pregnancy reduction were extracted for statistical analysis.

**Results:** Seventy-three women participated in the study. The mean age was 39 years and mean duration of infertility was 8.6 years. Only 3 (4.1%) respondents agreed to have SET as the overwhelming majority (70) 95.9% preferred 2 or more and they felt the more number of embryo transferred the better the chances of achieving pregnancy. Similarly most respondents, 38.4% (28) did not accept MFPR. Most respondents considered age (63%) and duration of infertility (78.1%) as major influencing factor for rejecting SET. Over 75% of respondents said they will still accept multiple embryos transferred despite knowledge of the possible complications.

**Conclusions:** While most infertile women in our sub region appear to recognize the risks with multiple pregnancy, they are less interested in SET or MFPR because they perceive more embryos transferred as a means to maximize treatment outcome. Government funding, client education and a blastocyst transfer protocol may improve acceptability as well as overall preference for less number of embryos transferred in our environment.

**Keywords:** Embryo transfer, Infertility, In-vitro fertilization, Multifetal pregnancy reduction, Multiple pregnancy, Single embryo transfer

### INTRODUCTION

The art and science of assisted reproduction technique has revolutionized infertility treatment worldwide, such that hitherto, some hopeless infertility conditions are now amenable to rewarding treatment with reported pregnancy rates of 10-18% and 30-35% for intrauterine insemination (IUI) and In-vitro Fertilization and Embryo Transfer (IVF-ET) respectively.<sup>1-3</sup> Consequent on the high cost of treatment (particularly IVF-ET), especially in the resource constraint setting of sub-Saharan Africa,

everyone including the provider and the patient is under immense pressure to achieve a high success rate. This quest has encouraged the transfer of multiple embryos at IVF-ET in order to enhance a successful outcome.<sup>4-6</sup>

While transfer of multiple embryos may be associated with increased pregnancy rates per cycle of treatment, it is also a cause of increased rates of multiple pregnancy which is considered as a treatment complication because of its attendant complications and ultimately decrease in the live birth rate.<sup>7,8</sup>

Multiple pregnancy, particularly the higher order multiple gestation is associated with increased risk of miscarriage and preterm delivery before 34 weeks of gestation.<sup>7-9</sup> Prematurity which is the main cause of neonatal morbidity and mortality occurs in almost half of multiple pregnancies. In one of the report, over 40% of women with twin pregnancies delivered before 37 weeks compared to less than 10% amongst singletons. The risk of perinatal mortality increased six folds in twins and 10-20 folds in triplets compared to singletons.<sup>9</sup> Even amongst neonatal survivors of preterm delivery, long term complications such as cerebral palsy and neurobehavioral disorders are major concerns to the family and society.<sup>10</sup>

As a result of the increased morbidity and mortality associated with multiple pregnancy, several documents have advocated the transfer of fewer embryos preferably one embryo (single embryo transfer: SET) in selected patients.<sup>11,12</sup> In 2003, De Sutter et al reported a significant reduction of multiple pregnancy with elective SET without a decline in the pregnancy rate.<sup>12</sup> There are other reports on the beneficial effects of elective SET in reducing multiple pregnancy rates in IVF programs without dropping the pregnancy rates.<sup>8,12,13</sup> Titinen and co-workers also reported reduced multiple pregnancy and a better cumulative pregnancy rates when SET is backed by embryo freezing program.<sup>14</sup> Despite the aforementioned risk of multiple pregnancies and the benefit of transferring fewer embryos, many infertile patients accessing IVF treatment would still desire multiple embryo transfer because of their strong desire to succeed at first attempt as well as the high cost of treatment particularly when there is no government funding. This is particularly true for sub-saharan Africa where in addition there exist a wide spread cultural acceptability and desire for multiple pregnancy hence the tendency for clinicians to encourage multiple embryo transfer at IVF-ET.<sup>6,15,16</sup>

Multifetal pregnancy reduction is another modality to mitigate the prevalence and attendant complications of multiple pregnancy associated with assisted reproduction. Owing to poor uptake of SET by IVF patients, clinicians have advocated multifetatal pregnancy reduction (MFPR) as a final strategy to reduce the morbidity and mortality associated with IVF created multiple pregnancy.<sup>17,18</sup> MFPR refers to willful termination of further development in one or more fetuses to reduce the number of viable fetuses to two or occasionally one. Despite the reported benefit of MFPR, acceptance of the procedure is still low for several reasons chief amongst these are psychological, sociological and ethical consideration.<sup>19</sup>

IVF services are becoming widespread in Nigeria, with the majority in private facilities and only few in Government institutions albeit still patient funded. The pressure to succeed at first attempt is high amongst clinician and patients' worldwide; particularly in settings where the cost of treatment is solely borne by the patients

like is the situation in Nigeria. The need to succeed as soon as possible would therefore impact on how an IVF patient perceives multiple gestation and all the interventions to reduce the complications. As IVF-ET is gaining prominence in Nigeria, it becomes appropriate to evaluate the attitude and acceptance of policies such as single embryo transfer and multifetal pregnancy reduction by clients assessing assisted reproduction in this region. This study is therefore aimed at establishing the perception, attitude and acceptance of infertile women to multiple pregnancy, single embryo transfer (SET) and multifetal pregnancy reduction (MFPR).

## METHODS

The study was a cross-sectional survey conducted at the IVF unit of the department of Obstetrics and Gynaecology of the University of Benin Teaching hospital and Graceland Medical Centre Benin City. The University of Benin teaching Hospital (UBTH) is one of the major public health institutions in Nigeria with facility and manpower to render IVF services to desiring infertile patients. Graceland Medical Centre (GMC) Benin City is a private health facility with services for assisted reproduction and gynaecologic endoscopy. The study received ethical approval from the hospital ethics and research committee.

The study was conducted over a twelve (12) month period April 2017 to March 2018. All patients recruited for IVF-ET at the UBTH and GMC during the study period who gave informed consent participated. The research instrument was a semi-structured self administered (interviewer guided) questionnaire designed in three sections; Section one is on demography including age and duration of infertility, Section two is on the knowledge of IVF procedure and its complications, Section three is on their perception, attitude and acceptability toward multiple pregnancy and its complications as well as their knowledge, attitude and perception to single embryo transfer and multifetal pregnancy reduction. After explanation of the study objectives as well as the processes involved in SET and MFPR, informed consent was obtained from willing women; they participated in the study in a private setting and were assured that all their information would remain confidential, and their names was not required on the questionnaires.

### Statistical analysis

The appropriately completed questionnaire was analyzed using the SPSS statistical package version 20. Result was aggregated into means and proportions as appropriate and presented as frequency tables and percentages. Subset analysis was performed to determine significant difference between groups and level of significance ( $p < 0/05$ ) was determined with the t-test and chi-square test as appropriate.

## RESULTS

Seventy-three women participated in the study. According to the below Table 1, the mean age was 39 years, a range of 28 to 53 years. The duration of infertility was between 2 and 22 years with a mean duration of 8.6 years. Majority were nulliparous 50.7% and 16% had previously delivered. Similarly majority, 74% had secondary infertility.

**Table 1: Demographic characteristics of participants.**

Variable	Frequency (n)	Percent(%)
<b>Age</b>		
Mean±SD	39.4±5.8	NA
Range	28-53	
<b>Duration of infertility</b>		
Mean ±SD	8.7±4.7	NA
Range	2-22	
<b>Parity</b>		
0	20	27.4%
0 <sup>+</sup>	37	50%
≥1	16	21.9%
<b>Education</b>		
Tertiary	67	91.8%
Secondary	6	8.2%
<b>Social class</b>		
High	68	93.2%
Middle	5	6.8%
<b>Previous children</b>		
Yes	13	17.8%
No	60	82.2%
<b>Previous IVF</b>		
Yes	32	43.8%
No	41	56.2%
<b>Infertility</b>		
Primary	19	26%
Secondary	54	74%

As per the below Table 2 about 70% of respondents had correct knowledge of IVF and associated risk or complications with IVF. These respondents were familiar

with the basic processes of IVF-ET as well as the possible complications like ovarian hyperstimulation syndrome and multiple pregnancies.

### *Preference and choice of embryo transfer and perception and attitude to SET and MFPR*

Clients choice of number of embryo to be transferred: 1.4% (one person) for only one embryo transfer; 16.4% (12) chose two embryos; 58.9% (43) chose three and 23.3% (17) chose four embryos.

Majority of respondents (58.9%) preferred 3 embryos transferred at IVF-ET, they also perceived 3 as the ideal number of embryo to be transferred. Only 3 (4.1%) respondents agreed to have single embryo transferred as the overwhelming majority (70) 95.9% preferred 2 or more and they felt the more number of embryo transferred the better the chances of achieving pregnancy. Although majority agreed that multiple pregnancy resulting from multiple embryo transfer could result in fetal loss and preterm delivery with eventual lesser live birth rate. Majority (60.3%) still declined single embryo transfer. According to the Table 3, 44 (60.3%) declined single embryo transfer, 16 (21.9%) agreed they will probably accept SET with embryo freezing guaranteed as backup. Similarly most respondents, 38.4% (28) did not accept multifetal pregnancy reduction, but 30.1% would probably consider it if guaranteed complication free.

**Table 2: Participants knowledge of IVF.**

Knowledge variable	Frequency (%)
<b>Knowledge of IVF</b>	
Correct	70 (95.9%)
Incorrect	3 (4.1%)
<b>Knowledge of complications of IVF</b>	
Correct	65 (89%)
Incorrect	8 (11%)
<b>Knows risk of multiple pregnancy</b>	
Correct	65 (89%)
Incorrect	8 (11%)

**Table 3: Participants acceptability of SET and MFPR.**

Variable	Definitely	Probably	Neutral	Probably not	Absolutely not
Accept SET	4 (5.5%)	10 (13.7%)	7 (9.6%)	8 (11%)	44 (60.3%)
Accept MFPR	4 (5.5%)	22 (30.1%)	12 (16.4%)	7 (9.6%)	28 (38.4%)
Scared of the Procedure of MFPR	18 (24.2%)	21 (28.8%)	18 (24.7%)	10 (13.7%)	6 (8.2%)
Accept MFPR if no complication	28 (38.4%)	18 (24.7%)	11 (15.1%)	2 (2.7%)	14 (19.2%)

**Factors that influence acceptability of SET or MFPR**

According to the Table 4, most respondents considered age (63%) and duration of infertility (78.1%) as major influencing factor for accepting multiple and rejecting single embryo transfer. Finance 61%, better chance of pregnancy 54.8% and culture 65.8% are the other reasons for preferring multiple embryo transfer and rejecting SET. Over 75% of respondents said they will still accept multiple embryos transferred despite knowledge of the possible complications.

Sub-analysis of age and duration of infertility as a measure of acceptability or not of SET and MFPR

showed that non acceptability of SET or MFPR was associated with an older mean age and longer duration of infertility in comparison to those that accepted, but the difference was not statistically significant.

**Table 4: Patients perception of factors influencing desire for multiple embryos.**

Variable	Frequency (n)	Percent (%)
Age	47	63
Infertility duration	57	78
Finances	45	61.6
To improve outcome	40	54.8
Culture and religion	48	65.8

**Table 5: Association of age and infertility duration to the acceptability of SET and MFPR.**

Variable SET	Accept SET (no)	Accept SET (yes)	P value
Age (mean±SD)	39.9±5.8	37.9±5.6	0.22
Duration of infertility (mean±SD)	8.9±4.7	7.8±4.6	0.40
MFPR	Accept MFPR (no)	Accept MFPR (yes)	P value
Age (mean±SD)	39.7±5.9	38.9±5.6	0.57
Duration of infertility (mean±SD)	9.1±4.8	8.0±4.5	0.32

SET: Single embryo transfer; MFPR: multifetal pregnancy reduction

**DISCUSSION**

It is established that higher complications exist with multiple pregnancy than singleton.<sup>7-9</sup> Higher order multiple pregnancy resulting from multiple number of embryo transferred, may ultimately result in lower live birth rate. In this study despite an overwhelming majority being knowledgeable of this risk they still preferred to have multiple embryo transferred. Specifically they declined elective single embryo transfer and multifetal pregnancy reduction as strategies to mitigate this complication. While single embryo transfer (SET) and multifetal pregnancy reduction (MFPR) have been used to reduce incidence of higher order multiple pregnancy and improve the live birth rate following IVF in Europe and America the acceptability of such strategies and protocol is not encouraging in sub-saharan Africa. We found that almost all our respondents declined SET while only about a third agreed to probably accept MFPR. The acceptance of MFPR is premised on the fact that pregnancy has been achieved and thus they may probably consider reducing number of fetuses from 4 or 5 to 2. In addition the possibility of accepting MFPR was on an assurance of it being a complication free procedure. The ideal choice of number of embryo to be transferred being three (3) for most respondents. This is quite different from the population in Western society where elective SET is routine and widely acceptable.<sup>20-21</sup> This attitude may be influenced by the Government funding of the ART through the health insurance scheme.<sup>22,23</sup> Same cannot be said of the situation in Africa where IVF is not covered

by insurance and therefore involves huge out-of-pocket cost. This assumption is buttressed in this study where respondents believed that finance may play a role in influencing preference for multiple embryo transferred. So that following painstaking savings for an expensive IVF procedure, the transfer of multiple embryos is hoped will maximize their chance for a successful treatment and answer the question of family size once and for all.

Other factors clients perceived influenced preference for multiple embryo transfer were advanced maternal age, increased duration of infertility, cultural and religious acceptability of multiple births as well as a believe that it will increase their chances of achieving pregnancy. In line with our findings previous research also noted that though clinicians view multiple pregnancy as a problem only few infertile women feel it's a concern.<sup>16</sup> Similarly the age and duration of infertility have been previously identified as negating factors on acceptance of SET while knowledge of complications of multiple pregnancy and previous experience with preterm delivery positively affected acceptance of MFPR and SET.<sup>13,15,16</sup> A summation of our review of the acceptability of SET and reduction of multiple fetuses in an infertility population showed that; while most women appear to recognize the associated risks, they are less interested in single embryo transfer because they perceive more embryos transferred as a path to early one time success. The small number of cases and the lack of both multivariate analyses and outcome data limit the power

and generalization of the clinical implications of our findings.

The desire and hope for a better and improved probability of pregnancy is a principal reason most women elect for transfer of multiple embryos against single embryo transfer. This may suggest that if clients are exposed to other possible factors such as blastocyst transfer, comprehensive chromosome screening (CCS) or preimplantation genetic screening (PGS) which provides greater opportunity for selection of more viable, better quality and genetically normal embryos and consequently improved pregnancy and live birth rate, then SET may be accepted. The quality of the embryo transferred is important in determining implantation and successful pregnancy.<sup>24, 25</sup> Thus in our setting where resources for chromosomal studies and pre-implantation genetic diagnosis is limited, effort is geared towards achieving a blastocyst stage transfer; This would help select better quality embryo and thus encourage acceptance of counsel for single or maximum of two embryo for transfer.

Government funding or support of IVF services in Nigeria that will result in reduced out-of-pocket cost on the client may improve acceptability of procedures such as SET and MFPR. Furthermore patient education and counseling decision may help in influencing decisions on number of embryo transferred. Previous research documented that educational materials in form of fact sheets, brochures, videos, interactive tools, and patient testimonials reviewing SET and the risks and complications associated with multiple births can help patients make an informed decision on the number of embryos to transfer.<sup>26</sup>

## CONCLUSION

As a consequence of assisted reproduction (IVF), rates multiple births have increased over the years. Despite the risks associated with higher-order multiple births and subsequent calls for single-embryo transfer (SET) or multifetal pregnancy reduction as the standard of care for good-prognosis; most infertility clients and clinicians in sub Saharan Africa still encourage transfer of multiple embryos. Major challenges identified include the strong desire of couples experiencing infertility demanding transfer of multiple embryos in order to maximize their chance for a successful treatment, especially with limited resources. Government funding, client education and a blastocyst transfer protocol may improve acceptability for SET and MFPR as well as preference for less number of embryos transferred in our environment.

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