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■ Original Research Article

Frozen Embryo Transfers in Sub-Saharan Africa: A Five-Year Retrospective Study at Nordica Fertility Centre, Lagos, Nigeria

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ABSTRACT

Embryo Transfers (FET) have gained popularity in recent years as an alternative or complementary option to fresh embryo transfers in In Vitro Fertilization (IVF) cycles. Frozen Embryo Transfers offer several benefits, such as lower cost versus repeat cycles, reduced stress, and better endometrial receptivity. Frozen Embryo Transfers are also indicated in cases where fresh transfers have been shown to give subpar results, such as in polycystic ovary syndrome (PCOS) and endometriosis patients. However, the evidence on the comparative success rates of FETs and fresh transfers is inconclusive, and the practice of FETs is not widespread in Sub-Saharan Africa. **Objectives**: To describe the socio-demographic characteristics, indications, trends and outcomes of FET cycles performed at Nordica Fertility Centre, Lagos, Nigeria, between 2018 and 2022. **Methodology**: This was a retrospective study of all FET cycles performed at Nordica Fertility Centre, Lagos, Nigeria, from January 2018 to December 2022. Data on patient age, parity, infertility diagnosis, number of frozen embryos transferred, implantation rate, clinical pregnancy rate, live birth rate and complications were collected and analyzed using descriptive statistics and Chi-square tests were employed to assess the associations between categorical variables. **Results**: A total of 444 FET cycles were performed during the study period with 290 (65.3%) being from own eggs and 154 (34.7%) from recipients. The patients' overall mean age was 39.2±5.8 years with mean age of 33.4±4.7 and 45.0±6.9 for own eggs and recipients, respectively. Fifty-two (17.9%) patients transferred one embryo, 166 (57.2%) patients transferred two embryos and 72 (24.8%) transferred three embryos while 10 (6.5%) patients transferred one embryo, 101 (65.6%) patients transferred two embryos and 43 (27.9%) transferred three embryos from own eggs and recipients, respectively for the FET procedure. The findings show that there is a significant (p=0.02) difference in the proportion of patients that transferred one, two or three embryos when own eggs and recipients are compared. Ninety-four (32.4%) FET cycles resulted in viable pregnancies (Positive) and 196 (67.6) FET cycles were unsuccessful (Negative) from own eggs. Forty-four (28.6%) FET cycles resulted in viable pregnancies (Positive) and 110 (71.4) FET cycles were unsuccessful (Negative) from recipients. The result shows that there is no significant difference in the proportions of Own eggs and recipients that had positive or negative outcome (p=0.41). The FET cycles using Own Eggs had a slightly higher success rate of approximately 32.41% compared to FET cycles using Donor eggs which had a success rate of approximately 28.57%. This study observed a notable increase in the number of FETs performed annually, reaching its peak in 2022. This trend aligns with global patterns reported by the Society for Assisted Reproductive Technology (SART), reflecting a growing acceptance and utilization of FET over time. **Conclusion**: Frozen Embryo Transfer is a safe and effective option for IVF patients in Sub-Saharan Africa, with comparable success rates to fresh transfers and lower risk of complications. It is especially indicated for patients with PCOS, endometriosis, and recurrent implantation failure.

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INTRODUCTION

Infertility and the difficult journey through it remain a challenge in sub-Saharan Africa. Infertility is a significant concern for couples worldwide, affecting approximately one in every 10 couples globally[1]. Modalities and protocols to improve outcomes and make it a more comfortable journey continue to be evaluated and discussed. In recent years, advancements in assisted reproductive technologies (ART) have provided new hope for individuals and couples facing infertility. Among these technologies, Frozen Embryo Transfer (FET) has gained popularity around the world due to its potential advantages, including improved success rates compared to fresh transfers [2-3]. A report stated that 1/3 of IVF cycles in the UK were FETs[4]. According to a registry report by ESHRE, there has been an increasing trend in the proportion of frozen embryo transfer (FET) cycles compared to fresh cycles in Europe. In 2017, the ratio stood at 49%, marking a notable rise from the 38% reported in 2014 [5]. The rising costs of freezing and thawing of embryos however may be a demerit for Frozen Embryo transfers.

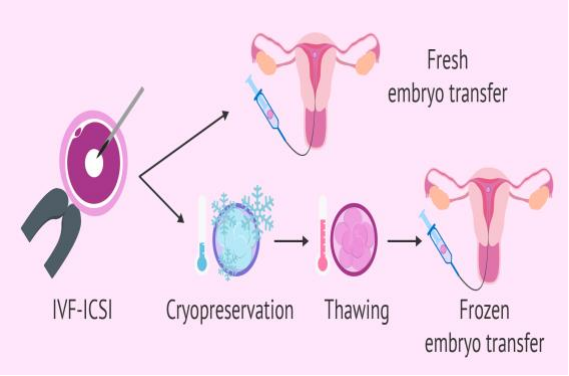

Figure 1: IVF - Fresh and Frozen Embryo Transfer Process.

Over the past ten years, there has been a swift rise in the prevalence of frozen-thawed embryo transfer (FET), constituting over 30% to 40% of total transfers in numerous regions worldwide[6-7]. Evidence has demonstrated that frozen-thawed embryo transfer (FET) yields comparable or potentially higher live birth rates than fresh embryo transfer[8]. Nevertheless, in comparison to fresh embryo transfer and spontaneous conception, frozen-thawed embryo transfer (FET) has been documented to be linked with elevated risks of pregnancy-induced hypertension, postpartum hemorrhage (PPH), and the birth of large-for-gestational-age (LGA) babies [9,10]. Over the last two years, there have been reports indicating a heightened risk of pregnancy-related hypertension following programmed frozen-thawed embryo transfer (FET) cycles. The absence of vasoactive corpus luteal products, such as relaxin, in programmed cycles has been proposed as a potential explanation for the compromised maternal cardiovascular adaptation during pregnancy, leading to the onset of hypertension [11-14]. Some of the suggested benefits and/or rationale for FET are to enable the woman's body to recover after Controlled Ovarian Stimulation (COH) and egg collection, reduces risk of Ovarian Hyperstimulation Syndrome (OHSS) allows the synchronization of the timing between embryo and endometrium to improve implantation, allows for PGT and preservation of fertility[15]. Batching/Cycle convenience, increased birth weight, reduced prematurity and reduced risk of placentation problems are also some of its benefits[16,17].

Despite the growing popularity of FET, there is a need for comprehensive studies to understand the factors influencing its success rates. This study aims to describe the socio-demographic characteristics, indications, trends and outcomes of FET cycles performed at Nordica Fertility Centre, Lagos, Nigeria, between 2018 and 2022. By examining these factors, we aim to gain insights into the dynamics of FET and this may be a valuable source of information for both patients and healthcare providers.

METHODOLOGY

This is a descriptive retrospective study of 444 consecutive cycles of FET carried out over a five-year duration at Nordica Fertility Centre, Lagos. Nordica Fertility Centre is a leading IVF centre in Nigeria, West Africa and the study took place between 2018 and 2022.

Data were collected from patient records, including age, occupation, Body Mass Index (BMI), indications for FET, number of embryos transferred, stage of transfer (Day 3 or Blastocyst), and success rates. Success rate refers to the proportion of successful outcomes, measured as the percentage of positive outcomes among the total number of Frozen Embryo Transfer (FET) cycles.

Descriptive statistics were used to summarize the demographic characteristics of participants. Chi-square tests were employed to assess the associations between categorical variables, such as age groups, BMI categories, indications for FET, transfer day, and pregnancy outcomes. Success rates were calculated based on the number of positive pregnancy tests (confirmation of pregnancy following the FET procedure) relative to the total number of FET cycles. All data obtained were entered and stored on Microsoft Excel, from which they were exported to STATA 16.0 software where statistical data analysis was performed.

RESULTS

Table 1 examines various factors related to Frozen Embryo Transfers (FET), including participant demographics, such as age, occupation, and body mass index (BMI), as well as indications for FET, transfer

Table 1: Comparison of Participant Demographics, Indications, and FET Outcomes Between Own Eggs and Recipient Eggs

Variable	Own		Recipient		χ^2	p-value
Age (years)	Number	Percent	Number	Percent		
20-29	61	21.0	0	-	189.52	0.0001
30-39	198	68.3	36	23.4		
40-49	31	10.7	80	51.9		
50-59	0	-	33	21.4		
60 and above	0	-	5	3.2		
Total	290	100	154	100		
$\bar{X}$ (SD.)	33.35 (4.73)		44.98 (6.88)			
Range	22-46		31-63			
Occupation						
Professional/Technical/Managerial	238	82.1	128	83.1	1.046	0.306
Clerical	1	0.3	2	1.3		
Sales and Services	4	1.4	1	0.6		
Skilled Manual	8	2.8	4	2.6		
Unskilled Manual	9	3.1	6	3.9		
Other	30	10.3	13	8.4		
Total	290	100.0	154	100.0		
Body Mass Index						
Underweight	2	0.8	0	-	6.930	0.008
Normal Weight	62	24.7	22	16.3		
Overweight	98	39.0	49	36.3		
Obese Class I	62	24.7	41	30.4		
Obese Class II	21	8.4	19	14.1		
Obese Class III	6	2.4	4	3.0		
Total	251	100.0	135	100.0		
$\bar{X}$ (SD.)	28.57(5.20)		30.29(5.09)			
Range	17-45		19-46			
Indications for FET						
PCOS	61	21.4	1	0.6	35.476	0.0001
Endometriosis or adenomyosis	27	9.5	7	4.4		
PGD/PGT	29	10.2	22	13.8		
Surrogacy	1	0.4	-	-		
Other	167	58.6	129	81.1		
Total	285	100.0	159	100.0		
Day 3 vs BT Transfer						
Day 3	111	38.3	46	29.8	10.615	0.014
BT	179	61.7	108	70.2		
Total	290	100.0	154	100.0		
Number of embryos transferred						
1	52	17.9	10	6.5	5.513	0.019
2	166	57.2	101	65.6		
3	72	24.8	43	27.9		
Total	290	100.0	154	100.0		
Outcome of FET						
Positive	94	32.4	44	28.6	0.693	0.405
Negative	196	67.6	110	71.4		
Total	290	100.0	154	100.0		

day, number of embryos transferred, and the outcomes of FET.

The study analyzed the ages of participants and found a significant difference between patients using own eggs and recipients of donor eggs (p=0.0001). In the 20-29 age group, there were 61 patients using own eggs, while no recipient of donor eggs was in this age group. Patients using own eggs were predominant in the 30-39 age group (198 patients) compared to recipients of donor eggs (36 patients). In the 40-49 age group, there were 31 patients using own eggs and 80 recipients of donor eggs. For patients aged 50-59, there were 33 recipients of donor eggs while none used own eggs. Similarly, for patients aged 60 and above, there were five recipients of donor eggs and no one used own eggs.

The occupation of participants did not show a significant difference in FET outcomes between those using own eggs and recipients of donor eggs (p=0.306). Most participants fell into the Professional/Technical/Managerial category, 82.1% and 83.1% for those using own eggs and recipients of donor eggs, respectively. This study found a significant difference in BMI between those using own eggs and recipients of donor eggs (p=0.008). Notably, in the "Underweight" category, only two patients using own eggs were observed, with no recipients of donor eggs. Patients using own eggs were more likely to fall into the "Normal Weight" (24.7%) and "Overweight" (39.0%) categories compared to recipients of donor eggs, while recipients of donor eggs were more likely to fall into the higher obesity classes (Class I (30.4%), II (14.1%), and III (3.0%)). The primary indications for FET varied significantly between patients using own eggs and recipients of donor eggs (p=0.0001). Polycystic Ovary Syndrome (PCOS) was a major indication for FET among those using own eggs with 61 cases, but only one recipient of donor eggs had PCOS. In contrast, other indications were more common among recipients of door eggs.

The timing of embryo transfer (Day 3 vs. BT) showed a significant difference in FET outcomes (p=0.014). Patients using own eggs were more likely to have a Day 3 transfer (111 cases) while recipients of donor eggs had fewer Day 3 transfers (46 cases). Conversely, recipients of donor eggs had a higher number of BT (blastocyst) transfers (108 cases), compared to patients using own eggs (179 cases). The number of embryos transferred also showed a significant difference in outcomes. Patients using own eggs were more likely to have two embryos transferred (166 cases), while recipients of donor eggs had fewer cases with two embryos (101 cases). Patients using own eggs also had more cases of three embryos transferred (72 cases) compared to recipients of donor eggs (43 cases).

The study did not find a significant difference in the outcomes of FET between patients using own eggs and recipients of donor eggs. Ninety-four FET cycles resulted in viable pregnancies (Positive) and 196 FET cycles were unsuccessful (Negative) with recipients of donor eggs while 44 FET cycles resulted in viable pregnancies (Positive) and 110 FET cycles were unsuccessful (Negative) with patients using own eggs.

Table 2 shows a clear comparison of the success rates of FET cycles between two groups: those using own eggs and recipients of donor eggs. The FET cycles using own eggs had a slightly higher success rate of approximately 32.41% compared to FET cycles of recipients of donor eggs which had a success rate of approximately 28.57%. This suggests that there is a difference in success rates between these two groups, with those using own eggs having a relatively higher success rate. This information is valuable for understanding the relative success of FET cycles using different sources of eggs and can provide insights for both patients and healthcare providers when considering fertility treatment options.

Table 2: Success Rates for the FET Study

Outcome of FET				Success Rate (%)
	Positive	Negative	Total	
Own eggs	94	196	290	32.41
Recipients	44	110	154	28.57

Figure 2 shows the trend in the number of FETs performed annually over a five-year period, from 2018 to 2022. In 2018, there were approximately 106 FETs performed. The number of FETs increased significantly in 2019, reaching around 166 procedures. This indicates a noticeable rise in the utilization of FETs between 2018 and 2019. In 2020, the number of FETs decreased slightly to approximately 138. While it is lower than the previous year, it is still higher than the starting point in 2018. The year 2021 saw a significant increase in the number of FETs, with approximately 212 procedures. This marks a clear upward trend in the utilization of FETs compared to the previous years and year 2022 experienced a substantial surge in the number of FETs, reaching around 319. This represents a remarkable increase, suggesting a growing preference for FET as a fertility treatment option. The line chart therefore indicates that the utilization of FETs has been on the rise over the five-year period of study while there were fluctuations from year to year, the general trend is an increase in the number of FETs performed, with a notable spike in 2022. This trend may reflect advancements in reproductive technology, increased awareness, and the growing acceptance of FET as an effective method for fertility treatment.

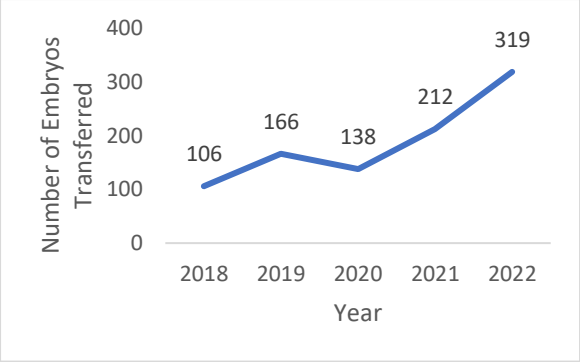

Figure 2: Annual Trends in Frozen Embryo Transfers (FETs) from 2018 to 2022

DISCUSSION

This study aimed to investigate the socio-demographic characteristics, indications, trends, and outcomes of Frozen Embryo Transfers (FETs) over a five-year period at Nordica Fertility Centre, Lagos, Nigeria. The study revealed a mean age of 39.2 years for patients undergoing FET, with distinctions between those using own eggs and recipients of donor eggs. The correlation between age and FET success rates is well-documented and findings of this study supports the understanding that age remains a crucial factor influencing FET outcomes[18]. Polycystic Ovary Syndrome (PCOS) emerged as a predominant indication for FET in this study. This is in consonance with the findings of a study recently published[19], which identified PCOS as a common indication for FET cycles. The prevalence of specific indications may differ across regions and populations, and this study contributes to the limited data available for Sub-Saharan Africa. In this study a notable increase in the number of FETs performed annually was observed, reaching its peak in 2022. This trend aligns with global patterns reported by the Society for Assisted Reproductive Technology (SART) [20], reflecting a growing acceptance and utilization of FET over time. The reasons for this increase warrant further study though it may be related to availability of advanced laboratory techniques and shift in patient preferences.

The overall success rate of FET cycles in this study was approximately 31.08%. This finding is above 30% and it falls within the range reported in the literature[21].

CONCLUSION

In conclusion, this study provides valuable insights into the dynamics of Frozen Embryo Transfer (FET) cycles in a cosmopolitan infertility treatment centre. It highlights the influence of demographic factors, indications for FET, timing of transfer, and the number of embryos transferred on the success rates of FET. These findings can assist both patients and healthcare providers in making informed decisions regarding fertility treatments. Further research is warranted to delve deeper into the factors that influence increasing uptake of FET and use of donor-egg despite prevailing cultural issues, as well as FET success and to develop personalized treatment strategies. The figures over the last three years (2020 – 2022) showed about 20% of all IVF cycles were FETs. This study observed a notable increase in the number of FETs performed annually, reaching its peak in 2022. This trend aligns with global patterns reported by the Society for Assisted Reproductive Technology (SART) [21], reflecting a growing acceptance and utilization of FET over time.

Based on the findings of this study, healthcare providers should consider tailoring FET treatment plans based on patient-specific factors, such as age, BMI, and indications for FET. The timing of embryo transfer (Day 3 vs. Blastocyst) should always be carefully evaluated to maximize the chances of a successful pregnancy. Patients should receive comprehensive counselling and support throughout the FET process to help them make informed decisions and manage expectations. Continued research into the factors influencing FET success is essential to refine treatment protocols and improve outcomes for further research.

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