Article

Not peer-reviewed version

Success Rate, Type of Delivery, and Neonatal Outcomes in Pregnancies Achieved Through Embryo Cryotransfer

Isabel María Guerrero Porras , Isaac Cohen Corcia * , Ana Cerezo Mondragon , Lorena Sabonet Morente , Ana Ruiz Martin , Isabel Castro Vega , Jesus Jimenez Lopez

Posted Date: 8 August 2025

doi: 10.20944/preprints202508.0589.v1

Keywords: frozen embryo transfer; infertility; assisted reproduction; obstetric outcomes; perinatal outcomes

 doi:10.20944/preprints202508.0589.v1

Article

Success Rate, Type of Delivery, and Neonatal Outcomes in Pregnancies Achieved Through Embryo Cryotransfer

Isabel María Guerrero Porras [1], Isaac Cohen Corcia [1,2,3,*], Ana Cerezo Mondragon [1,2], Lorena Sabonet Morente [1,2,3], Ana Ruiz Martin [4], Isabel Castro Vega [4] and Jesus S. Jimenez-Lopez [1,2,3]

[1] Department of Surgical Specialties, University of Malaga, 29010 Málaga, Spain
[2] Obstetrics and Gynecology Department, Hospital Materno-Infantil, Hospital Regional Universitario Málaga, Avenue Arroyo de los Ángeles S/N, 29011 Málaga, Spain
[3] Research Group in Maternal-Fetal Medicine Epigenetics Women's Diseases and Reproductive Health, Biomedical Research Institute of Malaga (IBIMA), 29071 Málaga, Spain
[4] Servicio de Laboratorio clínico. Embriologia. Hospital Materno-Infantil, Hospital Regional Universitario Málaga, Avenue Arroyo de los Ángeles S/N, 29011 Málaga, Spain
* Correspondence: icohenc@gmail.com

Abstract

Background: The use of assisted reproductive technologies, particularly frozen embryo transfer (FET), has become increasingly prevalent as a means to address infertility. This study aimed to evaluate the success rate, delivery type, and neonatal outcomes following FET in hormonally prepared cycles within a single tertiary center. **Methods:** We conducted a retrospective analysis of 275 women who underwent FET. Patient age, infertility factors, pregnancy outcomes, delivery type, and neonatal data—including birth weight and Apgar scores—were analyzed descriptively. **Results:** Pregnancy was achieved in 28.0% of FET cycles, with a singleton rate of 97.3%. Term births represented 70.7% of pregnancies, and cesarean delivery occurred in 29.3% of cases. Neonatal outcomes were favorable: in singleton pregnancies, 89.3% of newborns had a birth weight between 2,500–4,000g, and all neonates exhibited Apgar scores ≥7 at both one and five minutes. Multiple pregnancies were uncommon (2.7%) but associated with a higher frequency of low birth weight (<2,500g). **Conclusion:** FET is a safe and effective strategy for achieving pregnancy, with high rates of singleton gestations and positive perinatal outcomes. However, the retrospective, single-center design and limited sample size constrain the generalizability and the ability to assess rare outcomes.

Keywords: frozen embryo transfer; infertility; assisted reproduction; obstetric outcomes; perinatal outcomes

1. Introduction

Infertility is a growing global health concern, affecting approximately 15% of couples of reproductive age and posing significant medical, psychological, and social challenges. According to the World Health Organization (WHO), infertility is recognized not only as a disease but also as a public health priority, given its emotional burden and increasing prevalence worldwide. [1]

Over the past two decades, assisted reproductive technologies (ART) have evolved rapidly, with frozen embryo transfer (FET) emerging as a cornerstone technique. FET allows for the optimal use of surplus embryos generated during in vitro fertilization (IVF) cycles and offers several clinical advantages, including improved endometrial synchronization, reduced risk of ovarian hyperstimulation syndrome (OHSS), and better reproductive planning. Recent evidence also

 doi:10.20944/preprints202508.0589.v1

suggests that deferred embryo transfer may be associated with higher cumulative live birth rates compared to fresh transfer in certain populations [2].

Programmed FET cycles, which rely on hormone replacement therapy (HRT) for endometrial preparation, are particularly advantageous in clinical settings requiring cycle scheduling flexibility and precise embryo-endometrium timing. However, concerns remain regarding potential obstetric and perinatal risks associated with artificial endometrial preparation. Several studies have indicated a higher incidence of hypertensive disorders of pregnancy, abnormal placentation, and increased rates of cesarean delivery in programmed FET cycles [3,4]. In contrast, other data suggest that FET may reduce the risk of small-for-gestational-age (SGA) infants and prematurity when compared to fresh transfers [5,6].

Moreover, advances in cryopreservation techniques, particularly vitrification and re-cryopreservation, have enhanced embryo survival and pregnancy outcomes, but there is still debate on their impact on long-term neonatal health [7]. Studies published in the past three years emphasize the importance of individualized protocols based on maternal characteristics, previous ART outcomes, and embryo quality to improve both safety and efficacy [3–5].

Despite the extensive use of FET worldwide, there remains a need for local and context-specific data to assess how these outcomes translate into real-world clinical settings. Differences in population demographics, healthcare protocols, and ART access can significantly influence reproductive success and perinatal outcomes.

This study aimed to evaluate obstetric and neonatal outcomes following hormone-programmed FET cycles in a Spanish tertiary hospital during 2023, providing data that can be compared to international findings and inform future clinical guidelines. Additionally, it seeks to identify potential areas for improvement in embryo transfer protocols and contribute to the optimization of ART-related maternal and neonatal care.

2. Materials and Methods

2.1. Study Design

This study was designed as a retrospective observational cohort analysis based on clinical records from the Regional University Hospital of Málaga, a tertiary-level institution with a specialized reproductive medicine unit. It included all frozen embryo transfer (FET) cycles performed between January 1 and December 31, 2023.

The study protocol was developed in accordance with the principles of the Declaration of Helsinki and received approval from the Ethics Committee of the Provincial Centre of Málaga (Protocol Code: 2024-003215; Approval Date: January 22, 2025). All data were fully anonymized, and confidentiality was guaranteed throughout the data collection and analysis process.

2.2. Study Population

The study population comprised women who underwent programmed FET cycles using hormone replacement therapy (HRT) for endometrial preparation. Embryos were previously cryopreserved via vitrification and transferred at the blastocyst stage.

Inclusion criteria:

- Age ≥18 years.
- FET performed in hormonally prepared artificial cycles.
- Confirmation of clinical pregnancy by positive serum β-hCG followed by ultrasonographic visualization of an intrauterine gestational sac.

Exclusion criteria:

- Use of other assisted reproductive techniques (e.g., intrauterine insemination, fresh embryo transfer).
- Presence of active or uncontrolled infections (HIV, hepatitis B/C, syphilis).
- Uterine anatomical abnormalities incompatible with gestation.

 doi:10.20944/preprints202508.0589.v1

- Embryo transfers canceled due to endometrial asynchrony, endometrial cavity fluid, or technical failure during thawing.

These criteria were intended to ensure a homogeneous sample and to allow the isolated evaluation of outcomes derived specifically from hormone-prepared FET.

2.3. Variables and Data Collection

Clinical data were retrieved from the hospital's electronic medical record system (DIRAYA) and cross-validated by two independent researchers. The following variables were collected and categorized:

- **Maternal characteristics**: age at time of embryo transfer (stratified as <30, 30–35, and >35 years), and primary infertility etiology (male, ovarian, tubal, uterine, mixed, unexplained, single-parent/LGBTQ+, other).
- **FET cycle outcomes**: embryo transfer result (clinical pregnancy, no pregnancy, miscarriage before 20 weeks, or canceled cycle), number and quality of embryos transferred (where available), and endometrial thickness before progesterone initiation.
- **Pregnancy-related data**: gestational type (singleton or multiple), gestational age at delivery (term ≥37 weeks, preterm <37 weeks, very preterm <32 weeks), and mode of delivery (spontaneous vaginal, operative vaginal, or cesarean section).
- **Neonatal outcomes**: birth weight (categorized as <2500 g, 2500–4000 g, >4000 g), Apgar scores at 1 and 5 minutes, and neonatal intensive care unit (NICU) admission when documented.

All data were de-identified and stored in a secure, password-protected database. Missing or incomplete data were treated through listwise deletion given the non-inferential, descriptive nature of the study.

2.4. Statistical Analysis

Descriptive statistical analysis was conducted using IBM SPSS Statistics (version 27.0, IBM Corp., Armonk, NY, USA). Categorical variables were presented as absolute frequencies and percentages. Continuous variables were summarized using mean ± standard deviation (SD) or median with interquartile range (IQR), depending on the normality of distribution, assessed via the Shapiro–Wilk test.

No inferential testing was conducted, as the primary objective was to describe the clinical profile and outcomes of programmed FET cycles. Exploratory comparisons were performed to detect patterns or associations that could inform future hypothesis-driven studies.

3. Results

3.1. Population Characteristics

A total of 275 women were included in the study. Most participants were over 30 years old, with the largest proportion corresponding to the >35 years age group (45.1%), followed closely by those aged 30–35 years (44.4%). Women under 30 years represented a minority (10.5%). These data highlight that the study population predominantly comprised women of advanced reproductive age.

Table 1. Age Distribution. Percentage distribution of patients (n = 275) by age group.

Age Group	N	%
<30 years	29	10.50%
30–35 years	122	44.40%
>35 years	124	45.10%
Total	275	100%

 doi:10.20944/preprints202508.0589.v1

3.2. Etiology of Infertility

The most frequent etiology of infertility among the 275 women included in the study was male factor (41.7%), followed by mixed factor (24.7%). Ovarian factor accounted for 9.5% of cases, while single-parent/LGBTQ+ couples represented 7.6%. The origin of infertility was unknown in 8.7% of patients. Other less common causes included gynecological pathologies (4.7%), tubal factor (0.7%), and uterine factor (0.4%). These findings indicate that male and mixed etiologies predominate in this cohort.

Table 2. Etiology of infertility. Frequency and percentage of the main etiological factors of infertility in the total sample (n=275). Male factor was the most common cause, followed by mixed factor.

Cause	N	%
Male factor	115	41.70%
Mixed factor	68	24.70%
Ovarian factor	26	9.50%
Single-parent/LGBTQ+ couple	21	7.60%
Unknown cause	24	8.70%
Gynecological pathologies	13	4.70%
Tubal factor	2	0.70%
Uterine factor	1	0.40%

3.3. Frozen Embryo Transfer Outcomes

Of the 275 cycles analyzed, pregnancy was achieved in 77 cases, representing a pregnancy rate of 28.0%. The overwhelming majority of pregnancies were singleton (97.3%), whereas multiple gestations were uncommon (2.7%). No pregnancy occurred in 170 cycles (61.8%), and miscarriages were recorded in 20 cases (7.3%). In 8 cycles (2.9%), embryo transfer was not performed. These results reinforce the predominance of singleton pregnancies following FET in this cohort.

Table 3. Distribution of outcomes following embryo transfer (n = 275).

Category	N	%
Pregnancy achieved	77	28.00%
- Singleton	75	97.30%
- Múltiple	2	2.70%
No pregnancy	170	61.80%
Miscarriage	20	7.30%
No transfer	8	2.90%

Cesarean delivery accounted for 29.3% of births. Of the total pregnancies achieved, 70.7% reached term, which could be related to a more interventionist clinical approach in pregnancies conceived through assisted reproductive technologies.

3.4. Perinatal Outcomes

In In singleton pregnancies, the majority of newborns (89.3%) had a birth weight within the normal range (2,500–4,000 g), while low birth weight (<2,500 g) was observed in 10.7% of cases. No cases of macrosomia (>4,000 g) were recorded among singletons. Neonatal adaptation was excellent: all newborns from singleton pregnancies achieved Apgar scores of 7–10 at one minute and ≥7 at five minutes.

In contrast, multiple pregnancies showed a higher incidence of low birth weight, affecting 50% of newborns. The remaining 50% had weights in the normal range, with no cases of macrosomia. Despite the increased frequency of low birth weight, all infants from multiple pregnancies also demonstrated optimal adaptation, achieving Apgar scores of 7–10 at one minute and ≥7 at five minutes.

 doi:10.20944/preprints202508.0589.v1

Table 4. Birth weight and neonatal adaptation by type of pregnancy.

Type of Pregnancy	<2500 g	2500–4000 g	>4000 g	Apgar 1′ 7–10	Apgar 5′ ≥7
Singleton	10.70%	89.30%	0%	100%	100%
Múltiple	50%	50%	0%	100%	100%

4. Discussion

The results of our study confirm the male factor as the main cause of infertility (41.7%), in accordance with data previously reported in the literature. Our findings on frozen embryo transfer (FET) in programmed cycles align with recent research on advanced assisted reproductive techniques in terms of obstetric and neonatal safety of these procedures.

Moreover, the majority of pregnancies achieved were singleton (97.3%) and reached full term in 70.7%, supporting the clinical utility of the elective single embryo transfer (eSET) strategy. Both in our series and in the literature, we observed that FET in artificial cycles is associated with a high proportion of full-term singleton pregnancies and favorable neonatal outcomes, particularly in singleton gestations. These findings highlight the advantages of minimizing multiple pregnancies to reduce perinatal complications. [1–3]

In our cohort, 97.3% of pregnancies achieved via FET were singleton, and 70.7% reached full term—figures similar to those described in other contexts that emphasize the importance of elective single embryo transfer to minimize the risks associated with multiple gestations. [3,4]

Notably, our findings are consistent with the most recent study on embryo re-cryopreservation regarding the obstetric and neonatal outcomes of FET: both studies confirm that chemical and clinical pregnancy rates are comparable between conventional FET and advanced techniques or embryos subjected to double cryopreservation, maintaining high neonatal safety regarding low birth weight, malformations, and neonatal adaptation. [5,6]

Importantly, some studies have found a lower risk of small-for-gestational-age (SGA) newborns and placental abruption after FET compared to fresh cycles; however, a significantly higher risk of large-for-gestational-age (LGA) newborns and cesarean delivery in pregnancies conceived via FET has also been documented.

These results suggest that while FET improves certain perinatal and placental outcomes, it also entails a higher risk of macrosomia. [4–7]

An important finding—present in both this cohort and in the meta-analysis—is that the incidence of preeclampsia and other hypertensive complications may be higher after FET, although these findings require confirmation in further studies. [3,6] In our series, we did not observe a significantly higher incidence compared to the general population.

The cesarean section rate was high (29.3%), reflecting a tendency toward cautious management in pregnancies achieved through assisted reproduction, although it also suggests opportunities to optimize delivery mode based on individualized clinical criteria.

This conservative clinical approach impacting delivery method highlights the need to revise obstetric protocols to support a more individualized and less interventionist approach when feasible. [4,5]

Regarding neonatal outcomes, in singleton pregnancies, normal birth weight predominated (89.3% between 2500–4000 g), and excellent neonatal adaptation was observed (100% with Apgar ≥7 at one and five minutes). [2,3]

Although in multiple pregnancies a higher frequency of low birth weight was observed (50% <2500 g), neonatal adaptation at five minutes was optimal in all cases.

These findings are consistent with those of various authors [2,3,5,6], who reported no statistically significant differences in neonatal weight or the rate of congenital defects between groups with a history of cesarean or vaginal delivery.

 doi:10.20944/preprints202508.0589.v1

A relevant commonality among these studies is the identification of preterm birth as an outcome deserving attention.

Although our study reports 70.7% term pregnancies, other authors have indicated a higher risk of preterm birth after embryo transfer in women with a prior cesarean, especially in fresh transfers (RR 1.59, 95% CI: 1.16–2.19).

This finding suggests that obstetric history may influence perinatal outcomes and should be considered when planning embryo transfer. [2,3]

The cesarean rate in our cohort was 29.3%, reflecting a clinical tendency toward more interventionist management in pregnancies resulting from assisted reproduction.

Although our study did not specifically examine the influence of previous cesarean sections on FET outcomes, other studies provide evidence that this history may be associated with lower biochemical pregnancy and live birth rates, possibly due to altered endometrial receptivity or the presence of isthmocele. [2–4]

The overall success rate (28.0%) was lower than that reported in other series (30–40%), pointing to areas for improvement in embryo selection, endometrial preparation, and a more personalized approach.

In sum, FET management must be highly individualized, taking into account maternal risk factors, achieving the most physiological endometrial preparation possible, and transferring a single embryo to reduce maternal and perinatal complications, especially those associated with artificial cycles.

In line with our analysis, various studies recognize frozen embryo transfer as a safe technique with good perinatal outcomes, particularly in singleton pregnancies.

However, they also concur on the need to optimize factors such as endometrial preparation, embryo selection, and personalized follow-up to improve implantation and pregnancy rates.

This study has several limitations that should be considered when interpreting the results. Its retrospective design prevents establishing definitive causal relationships between the variables analyzed. Additionally, this is a single-center study conducted exclusively at the Regional University Hospital of Málaga, which may limit the generalizability of the findings to other populations or clinical contexts.

Finally, the sample size of 275 patients, although relevant in a hospital setting, may be insufficient to detect significant differences in specific subgroups such as multiple pregnancies or cases of low neonatal weight.

These limitations highlight the need for multicenter, prospective studies with greater statistical power to validate the results. [2–7]

5. Conclusions

This study provides a comprehensive evaluation of obstetric and neonatal outcomes following frozen embryo transfer (FET) in hormonally prepared cycles, based on real-world data from a single tertiary care center. FET proved to be a safe and effective assisted reproductive strategy, particularly in achieving singleton pregnancies with favorable perinatal outcomes. Among pregnancies achieved, 97.3% were singleton and 70.7% reached full term, with excellent neonatal adaptation, as reflected by Apgar scores ≥7 at both one and five minutes.

The most common etiology of infertility was male factor (41.7%), consistent with previous literature. The overall clinical pregnancy rate was 28%, which is slightly lower than that reported in comparable studies, suggesting opportunities for optimization in embryo selection, endometrial preparation, and transfer protocols.

A notable contribution of this study is its exclusive focus on programmed hormone replacement therapy (HRT) cycles, enabling a controlled assessment of their impact on clinical outcomes. This enhances the reliability of conclusions drawn regarding maternal and neonatal safety in this specific setting.

 doi:10.20944/preprints202508.0589.v1

However, several limitations must be acknowledged. The retrospective design limits the ability to establish causal relationships. Being a single-center study, external validity may be restricted. Moreover, the sample size, while adequate for descriptive analysis, may not be sufficient to detect differences in low-incidence outcomes such as neonatal complications or hypertensive disorders of pregnancy. Additionally, long-term neonatal outcomes were not evaluated.

Future research should focus on prospective, multicenter studies with larger and more diverse populations. These studies should assess the comparative effectiveness of different endometrial preparation strategies (natural vs. artificial cycles), incorporate advanced embryo selection techniques (e.g., morphological scoring, preimplantation genetic testing), and include longitudinal follow-up of neonatal development. Interventions aimed at reducing the cesarean section rate in pregnancies conceived through assisted reproductive technologies should also be explored.

In summary, programmed FET remains a clinically valuable and generally safe approach. However, continued refinement of protocols and personalized patient care are essential to further improve reproductive outcomes and reduce associated obstetric risks.

Author Contributions: I.M.G.P., J.S.J.-L. and I.C.C. drafted and designed the article; A.C.M., I.C.V., A.R.M. and L.S.M. reviewed the clinical case and the current literature; I.M.GP. and J.S.J.L, writing—original draft preparation; I.M.G.P., J.S.J.-L. and I.C.C., writing—review and editing; J.S.J.-L., I.C.C., A,R,M. and A.C.M. reviewed the article critically; I.C.C., A.C.M, A.R.m. and L.S.M. continued the patient follow-ups. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was approved by the Institutional Research Ethics Committee. This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the CEI de Provincial Centre of Malaga, Spain (protocol code 2024-003215 and date of approval 22 January 2025).

Informed Consent Statement: Written informed consent has been obtained from the patients to publish this paper.

Data Availability Statement: The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. World Health Organization. Infertility: a public health issue. Geneva: WHO; 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/infertility
2. Conforti A, Picarelli S, Carbone L, La Marca A, Venturella R, Vaiarelli A, Cimadomo D, Zullo F, Rienzi L, Ubaldi FM, Alviggi C. Perinatal and obstetric outcomes in singleton pregnancies following fresh versus cryopreserved blastocyst transfer: a meta-analysis. Reprod Biomed Online. 2021 Feb;42(2):401-412. doi: 10.1016/j.rbmo.2020.09.029.
3. Jing S, Li XF, Zhang S, Gong F, Lu G, Lin G. Increased pregnancy complications following frozen-thawed embryo transfer during an artificial cycle. J Assist Reprod Genet. 2019 May;36(5):925-933. doi: 10.1007/s10815-019-01420-1.
4. Conrad KP, von Versen-Höynck F, Baker VL. Pathologic maternal and neonatal outcomes associated with programmed embryo transfer: potential etiologies and strategies for prevention. J Assist Reprod Genet. 2024 Apr;41(4):843-859. doi: 10.1007/s10815-024-03042-8.

 doi:10.20944/preprints202508.0589.v1

5. Jiang Y, Jin L, Huang B, Wu L, Ren X, He H. Cumulative live birth rate and neonatal outcomes after early rescue ICSI: a propensity score matching analysis. Hum Reprod Open. 2023 Nov 23;2023(4):hoad046. doi: 10.1093/hropen/hoad046.
6. Riemma G, De Franciscis P, Torella M, Narciso G, La Verde M, Morlando M, Cobellis L, Colacurci N. Reproductive and pregnancy outcomes following embryo transfer in women with previous cesarean section: A systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2021 Nov;100(11):1949-1960. doi: 10.1111/aogs.14239.
7. He T, Xue X, Shi J. Effect of re-cryopreservation on pregnancy and neonatal outcomes: Analysis using propensity score matching. Int J Gynaecol Obstet. 2024 Feb;164(2):684-692. doi: 10.1002/ijgo.15023.