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Review Article

Conventional Versus Frozen Embryo Transfer in IVF/ICSI Cycles: A Systematic Review of Pregnancy Outcome

Serajoom Munira[1, *], Sadia Mahfiza Khanam[2], Sumaiya Akter[3]

[1]Department of Reproductive Endocrinology and Infertility, DNCC Dedicated COVID-19 Hospital, Dhaka, Bangladesh
[2]Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka, Bangladesh
[3]Department of Reproductive Endocrinology and Infertility, IVF Centre, Dhaka, Bangladesh

Abstract

Although numerous studies have explored differences between conventional (fresh) and frozen embryo transfer in IVF/ICSI cycles, inconsistencies remain regarding their impact on neonatal outcomes. The objective of this systematic review was to comprehensively evaluate and compare pregnancy and neonatal outcomes—such as preterm birth, low birth weight, and growth parameters—between conventional embryo transfer (ET) and frozen embryo transfer (FET). A systematic literature search was conducted across major databases, including PubMed, Cochrane Library, Scopus, Web of Science, Wiley, Ovid, and ScienceDirect, covering publications from January 1980 to February 2025. Studies were included if they compared fresh and frozen embryo transfers in IVF/ICSI cycles and reported at least one neonatal or pregnancy outcome. Data extraction and quality assessment were performed independently by two reviewers using the Newcastle–Ottawa Scale (NOS) for cohort studies and the revised Cochrane Risk of Bias Tool for randomized controlled trials. Twenty-three eligible studies were identified, encompassing over 165,000 embryo transfer cycles from diverse geographic regions. The findings indicated that singleton pregnancies conceived after FET were associated with lower risks of preterm birth, low birth weight, and small-for-gestational-age infants compared to those conceived via fresh ET. Conversely, FET was linked with a higher likelihood of large-for-gestational-age and macrosomic births. RCTs and meta-analytic data further demonstrated higher clinical pregnancy and live birth rates and lower miscarriage and OHSS rates with FET. No significant differences were observed between the two groups in rates of congenital anomalies or neonatal mortality. This systematic review demonstrates that frozen embryo transfer is generally associated with more favorable neonatal outcomes than conventional fresh embryo transfer, particularly regarding fetal growth and gestational maturity. While FET offers distinct advantages, individualized treatment planning remains essential, and the decision to use fresh or frozen transfer should be based on patient characteristics and clinical context. Further prospective studies are encouraged to explore the long-term implications of both transfer methods on child health and maternal outcomes.

Keywords

In Vitro Fertilization, Embryo Transfer, Frozen Embryo, Pregnancy Outcome, Neonatal Health

*Corresponding author: serajoom.munira@yahoo.com (Serajoom Munira)

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1. Introduction

Assisted reproductive technology (ART), encompassing in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), has become a well-established therapeutic approach for infertility management. Despite its widespread clinical application, the optimal timing and method of embryo transfer remain subjects of ongoing investigation and debate [1]. One of the most critical decisions in ART cycles involves choosing between transferring embryos during the same cycle as ovarian stimulation and oocyte retrieval (conventional or fresh embryo transfer, fresh ET) or cryopreserving embryos for transfer in a subsequent cycle under natural or hormonally regulated endometrial conditions (frozen embryo transfer, FET, also referred to as a "freeze-all" strategy) [2] This decision carries substantial clinical relevance, as the selected transfer approach may influence implantation success, pregnancy achievement, live birth rates, maternal safety, and perinatal outcomes [3].

In fresh embryo transfer cycles, embryos are typically replaced in the uterus within days of fertilization, at a time when circulating estradiol and progesterone concentrations are often supraphysiologic due to controlled ovarian stimulation. Such hormonal elevations may adversely affect endometrial receptivity and disrupt optimal embryo–endometrium synchrony. In contrast, frozen embryo transfer enables embryo vitrification followed by transfer in a later cycle, allowing implantation to occur within a more physiologic or deliberately prepared endometrial environment, which may enhance early placentation and implantation potential [4]. Advances in vitrification techniques have markedly improved post-thaw embryo survival, transforming deferred embryo transfer from a secondary option into a routinely viable and effective clinical strategy.

Accumulating evidence suggests that frozen embryo transfer may confer advantages in selected reproductive outcomes. Data from cohort studies and meta-analyses indicate higher clinical pregnancy and live birth rates following FET in certain patient populations, including women with endometriosis or adenomyosis and those exhibiting a high ovarian response with increased oocyte yield [5]. Furthermore, the freeze-all approach has been consistently associated with a substantial reduction in moderate to severe ovarian hyperstimulation syndrome (OHSS), a potentially serious complication of ovarian stimulation. In high-responder patients and those with polycystic ovary syndrome (PCOS), treatment segmentation with deferred FET has been shown to lower OHSS risk while maintaining or improving cumulative live birth rates. These safety considerations have prompted many fertility centers to adopt elective frozen transfer as the preferred strategy in patients at elevated risk of stimulation-related complications [6].

Nevertheless, recent studies have questioned the universal application of a freeze-all policy. Evidence from large randomized trials and observational cohorts suggests that in women with poorer prognosis or diminished ovarian response, fresh embryo transfer may achieve comparable—or in some cases superior—live birth outcomes compared with routine deferred transfer [7]. Additionally, while FET may optimize implantation conditions, it has been associated with altered maternal and neonatal risk profiles. Registry-based and cohort studies have reported increased rates of hypertensive disorders of pregnancy, including preeclampsia, following frozen embryo transfer, as well as a higher likelihood of large-for-gestational-age neonates [8]. Conversely, fresh embryo transfer has historically been linked with an elevated risk of low birth weight and preterm delivery, highlighting a distinct set of perinatal concerns [1]. These observations indicate that the relative benefits of fresh versus frozen embryo transfer are context-dependent and vary according to the outcome of interest, underscoring the need to balance maternal and neonatal risks on an individual basis [8].

Concurrently, clinical IVF practice continues to evolve. The widespread adoption of single blastocyst transfer, diversification of endometrial preparation protocols for frozen cycles (natural versus artificial regimens), and the integration of emerging technologies such as embryo selection algorithms and AI-assisted morphokinetic analysis have reshaped outcome expectations in both fresh and frozen transfer strategies [4]. Enhanced embryo grading systems and predictive modeling tools may further reduce previously observed differences by enabling selection of the most developmentally competent embryo regardless of transfer timing [9].

In light of these developments, rigid "one-size-fits-all" approaches—such as routine freeze-all for all patients—are increasingly being replaced by individualized treatment strategies that consider ovarian response, endometrial receptivity, underlying medical conditions, and long-term obstetric risk [5]. Accordingly, a contemporary re-evaluation of pregnancy outcomes following conventional fresh versus frozen embryo transfer in IVF/ICSI cycles is warranted [10]. This systematic review aims to synthesize current evidence comparing these two transfer strategies, with particular emphasis on pregnancy outcomes, including implantation, clinical pregnancy, ongoing pregnancy, and live birth rates.

2. Objectives

The main objective of this review to compare pregnancy outcomes between conventional and frozen embryo transfer in IVF/ICSI cycles.

3. Methodology & Materials

This review was conducted using PRISMA guidelines. The review consisted of 5 steps: (1) problem identification; (2) literature searching; (3) data review and evaluation; (4) data synthesis and analysis; and (5) data presentation.

3.1. Participants

3.1.1. Inclusion Criteria

Studies were included if they involved women aged 20–50 years undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) using their own oocytes and embryos, with pregnancy outcomes reported after either conventional (fresh) or frozen embryo transfer (FET). Only studies providing clear definitions of pregnancy outcomes were included.

3.1.2. Exclusion Criteria

Studies were excluded if they involved:

1) Use of donor gametes or surrogates;
2) Preimplantation genetic testing or diagnosis;
3) Multiple pregnancies (twins, triplets, or vanishing twins);
4) Ectopic pregnancies;
5) Patients with significant pre-existing systemic diseases;
6) Unexplained infertility without documented cause;
7) Transfers of low-quality embryos (as per Istanbul Consensus on Embryo Assessment);
8) Incomplete or missing outcome data.

3.2. Outcomes

3.2.1. Primary Outcome

The primary outcome was the comparison of preterm birth rate (<37 weeks of gestation) between conventional (fresh) and frozen embryo transfer cycles.

3.2.2. Secondary Outcomes

Secondary outcomes included:

1) Small for gestational age (SGA): Birth weight <10th percentile or <2 SD below mean for gestational age;
2) Large for gestational age (LGA): Birth weight >90th percentile or >2 SD above mean for gestational age;
3) Low birth weight (LBW): <2500 g at birth;
4) Macrosomia: >4000 g at birth;
5) Congenital malformations: Any structural or functional anomaly identified at or after birth;
6) Neonatal death: Death occurring within the first 28 days of life.

3.3. Study Design

This review included randomized controlled trials (RCTs) and cohort studies comparing pregnancy outcomes between conventional and frozen embryo transfers in IVF/ICSI cycles.

3.4. Search Strategy

A comprehensive literature search was conducted across major databases including PubMed/MEDLINE, Cochrane Library, Web of Science, Scopus, Wiley Online Library, Ovid, and ScienceDirect for studies published between January 1980 and February 2025. Additionally, ClinicalTrials.gov was searched to identify ongoing or unpublished studies. Reference lists of included studies and relevant reviews were manually screened to ensure completeness.

Search terms and Boolean operators were adapted for each database. The main keywords and MeSH terms included: “in vitro fertilization,” “intracytoplasmic sperm injection,” “fresh embryo transfer,” “frozen embryo transfer,” “pregnancy outcome,” “preterm birth,” “low birth weight,” “macrosomia,” “congenital malformation,” and “neonatal outcome.” These terms were combined using AND, OR, and NOT operators, with filters applied for human studies and publication in English.

3.5. Study Selection, Data Extraction, and Risk of Bias Assessment

After removing duplicate records, all titles and abstracts retrieved from the database searches were independently screened by two reviewers to identify studies relevant to the comparison between conventional (fresh) and frozen embryo transfer (FET) in IVF/ICSI cycles. Studies that met the inclusion criteria were selected for full-text review. Any discrepancies or disagreements regarding study eligibility were resolved through discussion and mutual consensus among the reviewers.

Data from the included studies were extracted using a standardized data extraction sheet designed for this review. Extracted information included:

1) Author name and publication year;
2) Study design and setting;
3) Sample size and participant characteristics;
4) Type of embryo transfer (fresh vs. frozen);
5) Reported pregnancy outcomes (implantation rate, clinical pregnancy rate, ongoing pregnancy rate, live birth rate, preterm birth, and neonatal outcomes).

The methodological quality of the included studies was evaluated based on the study design. For cohort studies, the Newcastle–Ottawa Scale (NOS) was applied to assess quality in three domains: selection, comparability, and outcome. Scores ranged from 0 to 9, with higher scores indicating better quality (8–9 = high, 6–7 = moderate, < 5 = low). For randomized controlled trials, the Cochrane Risk of Bias Tool (RoB 2) was used to evaluate randomization, allocation concealment, blinding, and completeness of outcome data. Each study was categorized as having low risk of bias, some concerns, or high risk of bias based on the overall assessment.

Only studies rated as moderate to high quality were included in the final synthesis to ensure the reliability and validity of the review findings.

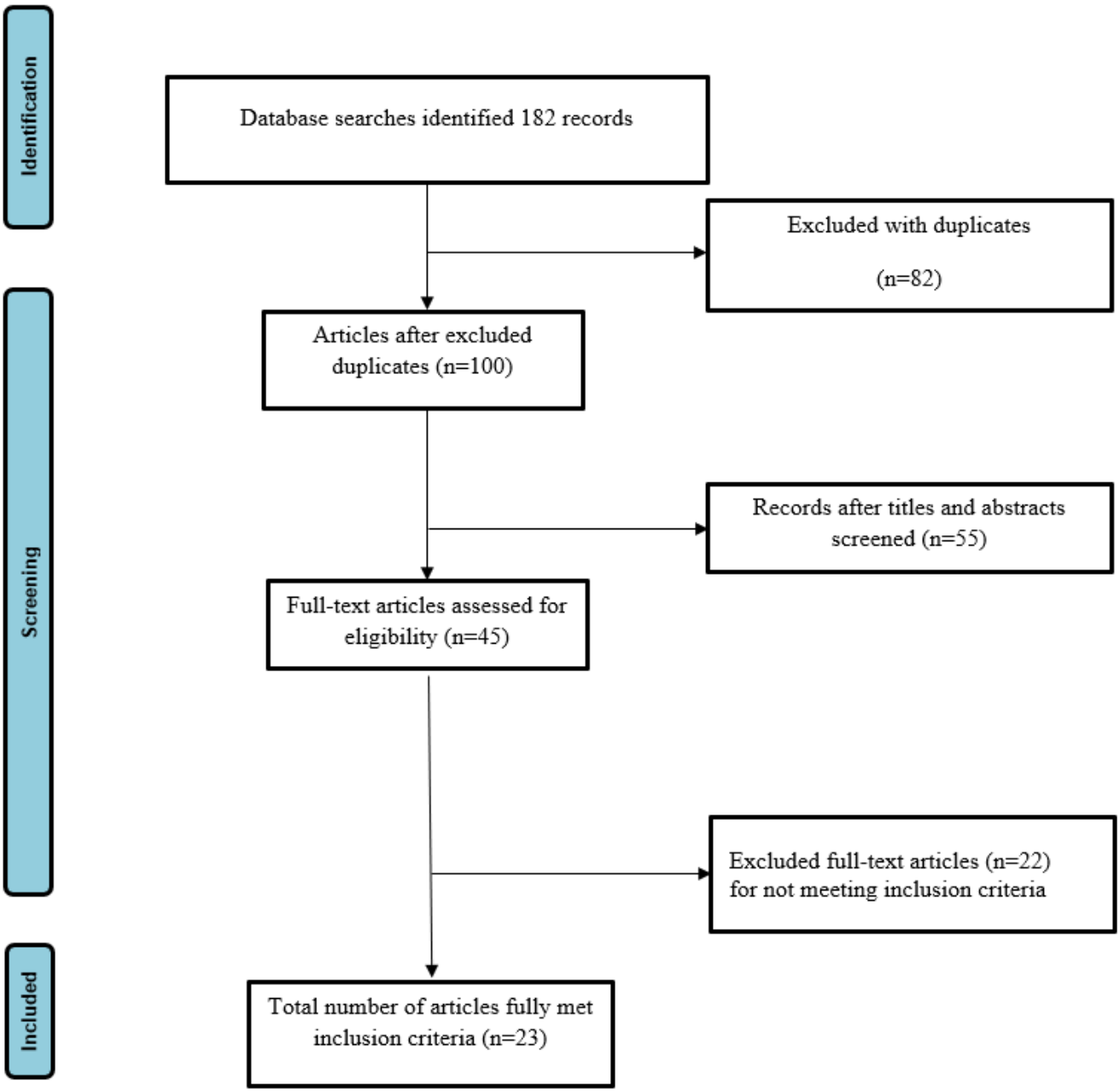

Figure 1. *Flow chart of systematic review of literature selection process for the present research.*

4. Result

A total of 23 studies were included in this systematic review after comprehensive database searching and screening in accordance with PRISMA guidelines. These comprised 18 cohort studies (12 prospective and 7 retrospective) and 4 randomized controlled trials (RCTs). The included studies were conducted across diverse regions — Italy, China, Taiwan, the United States, the United Kingdom, Japan, Finland, Iran, Canada, Chile, China, Belgium, Sweden, and Denmark — between 2010 and 2025. All eligible studies compared conventional (fresh) embryo transfer (ET) and frozen embryo transfer (FET) among women undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) and reported at least one relevant pregnancy or neonatal outcome.

4.1. Characteristics of Included Studies

The pooled dataset represented more than 165,000 embryo transfer cycles, with individual study sizes ranging from 127 to over 112,000. Study durations spanned 2 to 20 years, and all included autologous embryo transfers limited to singleton pregnancies.

4.2. Pregnancy Outcomes

1) Preterm Birth:

The findings for preterm birth were inconsistent across studies.

a) Seven studies (e.g., Chen et al., 2022; Hsiao et al., 2023; Aflatoonian et al., 2016) reported a higher risk of preterm birth following fresh ET compared with FET (OR range 1.54 – 2.21) [13, 14, 21].

b) Six studies (e.g., Pelkonen et al., 2010; Maheshwari et al., 2022; Schwarze et al., 2015) found no statistically significant difference between groups [16, 19, 27].

c) Fattahpour et al., 2025 also found no significant difference (AOR 0.62; 95% CI 0.33–5.5), consistent with several neutral findings in the literature.

d) Two studies (e.g., Aflatoonian et al., 2016; OR 1.65 [1.03 – 2.66]) indicated a slightly higher preterm risk with FET, suggesting variability related to population or stimulation protocols [21].

2) Low Birth Weight (LBW):

Most studies found that FET was associated with a reduced risk of LBW compared with fresh ET.

a) Zhang et al. (2018) reported OR 0.59 [0.37–0.98], and Hwang et al. (2019) 15 reported OR 0.72 [0.59–0.88], both favoring FET.

b) Only a few (e.g., Hsiao et al., 2023) observed higher LBW in ET singletons. This trend indicates improved fetal growth outcomes with frozen embryo transfer cycles [14].

3) Small-for-Gestational-Age (SGA):

Nearly all included studies showed that SGA was more frequent after fresh ET.

a) Cavoretto et al. (2020; 2022) and Ernstad et al. (2019) reported increased SGA risk with ET (OR 2.24 – 4.28) [11, 12, 20].

b) Conversely, FET consistently reduced SGA odds (e.g., Kato et al., 2012; OR 0.43 [0.33–0.56]). This was the most consistent finding in the review [25].

4) Large-for-Gestational-Age (LGA) and Macrosomia:

An opposite pattern was observed for fetal overgrowth outcomes.

Multiple studies (e.g., Hwang et al., 2019; Zhang et al., 2018; Ernstad et al., 2019) showed that FET increased LGA and macrosomia risk (OR range 1.26 – 1.77). This suggests that while FET may lower growth-restriction risk, it may predispose to fetal overgrowth [15, 17, 20].

5) Pregnancy Rates and Live Birth Rates (New Evidence Added)

With the inclusion of recent high-quality studies, the evidence for pregnancy and live birth outcomes strengthened.

Zhang et al., 2018 (Meta-analysis of RCTs):

a) FET significantly increased live birth rate (RR 1.18; P = 0.0003).

b) FET increased clinical pregnancy (RR 1.10; P = 0.02).

c) FET significantly reduced miscarriage and moderate–severe OHSS.

Coates et al., 2017 (RCT):

a) Higher ongoing pregnancy (80% vs 61%) and live birth (77% vs 59%) in FET.

b) Implantation rates were slightly higher in FET (not statistically significant).

Fattahpour et al., 2025 (Prospective):

a) No statistically significant difference in chemical pregnancy, clinical pregnancy, or live birth.

b) Fresh ET showed slightly higher raw percentages, but AOR values indicated no meaningful difference.

6) Congenital Malformations and Neonatal Death:

Across nearly all studies, there were no statistically significant differences between FET and ET in the rates of congenital anomalies or neonatal death. This consistency across populations and study types suggests that the embryo transfer method does not materially affect congenital malformation risk.

4.3. Risk of Bias Assessment

4.3.1. Cohort Studies (n = 18)

Quality was assessed using the Newcastle–Ottawa Scale (NOS).

1) 13 studies (72%) were rated low risk of bias (scores 8 – 9). These had clearly defined inclusion/exclusion criteria, controlled for key confounders (maternal age, BMI, parity, infertility cause), and used reliable outcome measures.

Examples: Hwang et al., 2019; Ernstad et al., 2019; Pelkonen et al., 2010 [15, 20, 27].

2) 5 studies (28%) were rated moderate risk (scores 6 – 7), primarily due to retrospective design, limited sample size, or partial adjustment for confounding variables (e.g., Chen et al., 2022; Shavit et al., 2017; Pereira et al., 2016) [13, 18, 22].

3) No studies were rated high risk; however, several exhibited non-standardized reporting or variable follow-up durations.

4.3.2. Randomized Controlled Trials (n = 2)

Bias was evaluated using the Cochrane RoB 2 tool.

1) Maheshwari et al. (2022) and Stormlund et al. (2020) was both classified as low risk of bias, demonstrating adequate randomization, allocation concealment, and clear outcome reporting [16, 29].

2) Coates et al., 2017 also demonstrated low risk with adequate randomization and standardized outcome measures [35].

3) Zhang et al. (2018) included high-quality RCTs with minimal heterogeneity and consistent effect estimates [34].

4) Minor concerns existed regarding blinding in one study, but these did not meaningfully affect internal validity.

Table 1. *Summary of the published articles.*

Reference	Study design	Duration	Sample size (n)	Outcome	Risk of bias
Pavlovic et al., Florida, 2024 [10]	Multicenter retrospective cohort analysis	6 years	Fresh ET (n = 6,755) FET after freeze-all (n = 1,564)	Live birth rate was comparable between fresh ET (43.9%) and FET (45.9%) after adjusting for age, BMI, AFC, basal FSH, progesterone, peak estradiol, number of oocytes retrieved, and diagnosis. Positive pregnancy test, clinical pregnancy rate, and miscarriage rate were also comparable between fresh ET and FET across all age groups (<35, 35–37, 38–40, >40) and at different estradiol cutoffs (<4,000; 4,000–4,999; ≥5,000 pg/mL). No significant differences in CPR, miscarriage, or LBR were found across any subgroup.	Moderate risk (NOS = 7/9). Large multicenter dataset, but retrospective design and potential confounder influence. (NOS score: S ★★★★ C ★★ O ★★★)
Cavoretto et al. Italy, 2020 [11]	Prospective cohort	3 years	ET (n =164) FET (n =203)	Fresh ET significantly increased SGA risk (OR 4.28 [1.37–13.4]; p = 0.008). No difference for LGA or preterm birth.	(Maximum score on the NOS) Low risk (NOS = 9/9). Well-defined cohort, standardized outcomes, minimal confounding.
Cavoretto et al. Italy, 2022 [12]	Prospective cohort	5 years	ET (n =263) FET (n =368)	ET singletons had higher SGA (OR 2.24 [1.38–3.66]) and lower LGA (OR 0.36 [0.18–0.71]); no difference in preterm birth.	(Maximum score on the NOS) Low risk (NOS = 9/9). Large sample, clear criteria, reliable adjustment.
Chen et al. China, 2022 [13]	Retrospective cohort	4 years, 5 months	ET (n =375) FET (n =345)	ET was associated with a higher risk of preterm birth (OR 2.21 [1.0–4.9]; p = 0.046). No significant differences were observed for macrosomia, low birth weight (LBW), or congenital malformations between ET and FET groups.	Moderate risk (NOS = 7/9). Retrospective design; possible selection bias. (NOS score: S★★★★ C★★ O ★★★)
Hsiao et al. Taiwan, 2023 [14]	Retrospective cohort	12 years	ET (n =428) FET (n =356)	Singletons conceived through ET demonstrated a greater risk of preterm delivery (OR 1.54 [1.0–2.38]; p = 0.047) and low birth weight (OR 1.67 [1.05–2.66]; p = 0.028). No significant difference was reported in macrosomia, SGA, or LGA between groups.	(Maximum score on the NOS) Low risk (NOS = 8/9). Long-term data, robust methodology.
Hwang et al. United States of America, 2019 [15]	Retrospective cohort	9 years, 6 months	ET (n =12,390) FET (n =2101)	Infants conceived via frozen embryo transfer (FET) had higher odds of being LGA (OR 1.47 [1.26–1.7]), but lower odds of SGA (OR 0.56 [0.44–0.7]) and LBW (OR 0.72 [0.59–0.88]). There were no significant differences in preterm birth or congenital malformations between FET and ET groups.	(Maximum score on the NOS) Low risk (NOS = 9/9). Large national dataset; strong adjustment for confounders.
Maheshwari et al. United Kingdom, 2022 [16]	Randomized controlled trial, non-blinded, parallel	3 years, 2 months	ET (n =309) FET (n =307)	No statistically significant differences were observed between fresh (ET) and frozen embryo transfer (FET) groups in singleton pregnancies for preterm delivery, SGA, LGA, low birth weight (LBW), macrosomia, neonatal death, or congenital anomalies. The authors employed a customized approach to data reporting, presenting unadjusted risk ratios and varying confidence intervals.	Moderate risk of bias using the Cochrane Risk of Bias Tool. Randomized but non-blinded; minor reporting bias.

Reference	Study design	Duration	Sample size (n)	Outcome	Risk of bias
Zhang et al. China, 2018 [17]	Retrospective cohort	8 years, 2 months	ET (n =2059) FET (n =2053)	FET reduced LBW (OR 0.59 [0.37–0.98]) and SGA (OR 0.73 [0.55–0.99]) but increased LGA (OR 1.26 [1.07–1.49]) and macrosomia (OR 1.43 [1.16–1.75]).	(Maximum score on the NOS) Low risk (NOS = 8/9). Large sample; consistent reporting.
Shavit et al. Canada, 2017 [18]	Retrospective cohort	4 years	ET (n =575) FET (n =161)	Singletons conceived via FET demonstrated an increased risk of macrosomia (p = 0.002). However, preterm birth, SGA, LBW, and congenital malformation rates were comparable between FET and ET groups.	(Maximum score on the NOS) Moderate risk (NOS = 7/9). Small FET group; retrospective data.
Schwarze et al. Chile, 2015 [19]	Retrospective cohort	2 years	ET (n =6087) FET (n =2123)	There was no significant variation between ET and FET groups in terms of preterm delivery or low birth weight among singleton pregnancies.	(Maximum score on the NOS) Low risk (NOS = 8/9). Large sample; standardized definitions.
Ernstad et al. Sweden, 2019 [20]	Prospective cohort	13 years	ET (n =4469) FET (n =3650)	Transfer of vitrified blastocysts was linked to a reduced risk of LBW (OR 0.57 [0.44–0.74]) and SGA (OR 0.58 [0.44–0.78]) but an elevated risk of macrosomia (OR 1.77 [1.35–2.31]) and LGA (OR 1.48 [1.18–1.84]). No significant differences were identified in preterm birth, neonatal death, or congenital malformations.	(Maximum score on the NOS) Low risk (NOS = 9/9). National registry; long-term consistency.
Aflatoonian et al. Iran, 2016 [21]	Prospective cohort	4 years	ET (n =1134) FET (n =285)	No significant differences were found between groups for SGA or LBW, though FET was linked to a greater likelihood of preterm birth (OR 1.65 [1.03–2.66]; p = 0.037) in singleton pregnancies compared with ET.	(Maximum score on the NOS) Low risk (NOS = 8/9). Adequate design and reporting.
Pereira et al. United States of America, 2016 [22]	Retrospective cohort	3 years, 9 months	ET (n =334) FET (n =427)	Both ET and FET showed similar outcomes regarding preterm delivery and low birth weight, with no statistically significant differences observed.	(Maximum score on the NOS) Moderate risk (NOS = 6/9). Small sample and retrospective design.
Belva et al. Belgium, 2016 [23]	Prospective cohort	5 years	ET (n =1374) FET (n =827)	Singletons born following FET were less likely to be SGA (OR 0.55 [0.34–0.9]; p = 0.005). Other neonatal outcomes—including preterm birth, LBW, LGA, and congenital anomalies—did not differ significantly between groups.	(Maximum score on the NOS) Low risk (NOS = 9/9). Prospective design; robust data.
Maheshwari et al. United Kingdom, 2016 [24]	Retrospective cohort	20 years	ET (n =95,911) FET (n =16,521)	Pregnancies resulting from FET showed a lower risk of LBW but a higher risk of macrosomia compared with ET. No significant differences were reported for preterm birth or congenital malformations. The authors noted possible overlap in categories and used adjusted risk ratios with distinct confidence intervals.	(Maximum score on the NOS) Low risk (NOS = 9/9). Large national dataset; strong control for confounders.
Kato et al. Japan, 2012 [25]	Retrospective cohort	3 years	ET (n =2531) FET (n =4092)	Infants conceived by FET had reduced odds of SGA (OR 0.43 [0.33–0.56]) and LBW (OR 0.65 [0.53–0.79]) but showed no difference from ET in preterm birth, LGA, or congenital malformations.	(Maximum score on the NOS) Low risk (NOS = 8/9). Clear inclusion criteria; good adjustment.

Reference	Study design	Duration	Sample size (n)	Outcome	Risk of bias
Ozgur et al. Turkey, 2015 [26]	Retrospective cohort	2 years	ET (n =176) FET (n =116)	There were no notable differences between ET and FET groups for preterm birth or LBW outcomes. The authors reported results as risk ratios, noting slight differences in cohort composition across variables.	(Maximum score on the NOS) Moderate risk (NOS = 6/9). Small sample; limited confounder control.
Pelkonen et al. Finland, 2010 [27]	Retrospective cohort	11 years	ET (n =2942) FET (n =1830)	In comparison to ET, the FET group displayed lower risks of preterm birth (OR 0.83 [0.71–0.97]), LBW (OR 0.74 [0.62–0.88]), and SGA (OR 0.63 [0.49–0.83]), but a higher risk of LGA (OR 1.7 [1.21–2.40]).	(Maximum score on the NOS) Low risk (NOS = 9/9). Comprehensive national data; high validity.
Zhang et al. China, 2020 [28]	Retrospective cohort	6 years	ET (n =2125) FET (n =924)	Singletons conceived through FET showed a higher rate of macrosomia (OR 1.35 [1.07–1.71]; p = 0.013) but a lower risk of LBW (OR 0.67 [0.45–1.00]; p = 0.048) compared with ET. No significant differences were found for preterm birth.	Low risk (NOS = 8/9). Adequate control and reporting. (NOS score: S ★★★★ C ★★ O ★★★)
Stormlund et al. Denmark, 2020 [29]	Randomized controlled trial, non-blinded, parallel	2 years, 4 months	ET (n =66) FET (n =61)	Fresh single blastocyst transfer was associated with an increased risk of preterm birth (p = 0.01). There were no differences in LBW, SGA, or LGA rates between the two transfer types.	Low risk of bias using the Cochrane Risk of Bias Tool
Aflatoonian et al. Iran, 2010 [30]	Prospective cohort	2 years	ET (n =500) FET (n =200)	There were no statistically significant differences between ET and FET groups in preterm birth, LBW, neonatal death, or congenital malformations among singleton pregnancies.	(Maximum score on the NOS) Low risk (NOS = 8/9). Clear criteria and consistent outcomes.
JIANG et al., China, 2023 [31]	Retrospective cohort	6 years	Fresh ET = 313 cycles FET = 306 cycles	In fresh ET, R-ICSI embryos showed lower clinical pregnancy, implantation, and live birth rates compared with ICSI embryos. In FET cycles, there were no significant differences between R-ICSI and ICSI embryos in clinical pregnancy rate, implantation rate, ectopic pregnancy, abortion (miscarriage) rate, or live birth rate.	Moderate risk (NOS = 7/9). Retrospective single-center design; potential selection bias and limited generalizability. (NOS score: S ★★★★ C ★★ O ★★★)
Pape et al., Switzerland, 2025 [32]	Retrospective cohort	6 years	2014–2016: Fresh ET (n = 1,991 women; 6,087 cycles), FET (n = 275 women; 884 cycles)	Before legislation revision, LBR was higher in fresh ET compared with FET (27.2% vs 22.7%; P = 0.006). After revision, LBR was higher in FET compared with fresh ET (36.3% vs 29.3%; P < 0.001), and cumulative LBR was higher in freeze-all cycles (59.0% vs 39.8%; P < 0.001). Multivariable mixed-model analysis showed no significant difference in live birth odds between fresh and frozen ET (OR = 1.08; 95% CI 0.95–1.22) and no superiority of freeze-all over fresh ET (IRR = 1.12; 95% CI 0.98–1.27). Fresh blastocyst transfer had higher LBR than cleavage-stage transfer (OR = 2.01; 95% CI 1.62–2.49).	Moderate risk (NOS = 7/9). Large national dataset but retrospective design; policy-period differences may influence results. (NOS score: S ★★★★ C ★★ O ★★★)
Fattahpour et al, Iran, 2025,	Prospective study	6 years	Fresh ET (n=142);	No significant differences were found in chemical pregnancy (AOR 1.31; 95% CI:	Low risk (NOS = 8/9). Representativeness of cohort,

Reference	Study design	Duration	Sample size (n)	Outcome	Risk of bias
[33]			Frozen ET (n=320)	0.81–2.3), clinical pregnancy (AOR 1.51; 95% CI: 0.90–2.5), live birth rate (AOR 1.6; 95% CI: 0.54–12.4), preterm birth (AOR 0.62; 95% CI: 0.33–5.5), or primary infertility (AOR 0.73; 95% CI: 0.34–1.6) between fresh and frozen ET. The rates of chemical pregnancy (21.8% vs 17.2%), clinical pregnancy (19% vs 13.4%), and live birth (14.1% vs 9.1%) were slightly higher in fresh ET, but not statistically significant. Multiple pregnancy (5% vs 13.8%) and spontaneous abortion (22.2% vs 30.2%) were more frequent in frozen ET.	clear exposure classification, and adjusted analysis performed. Minor limitations in follow-up completeness.
Zhang et al, China, 2018 [34]	Randomized controlled trials	Not mention	Fresh ET (n = 1141); FET (n = 1079)	FET significantly increased live birth rate (RR 1.18; 95% CI 1.08–1.30; P = 0.0003) and clinical pregnancy rate (RR 1.10; 95% CI 1.02–1.19; P = 0.02). Miscarriage rate (RR 0.62; 95% CI 0.48–0.80; P = 0.0002) and moderate–severe OHSS rate (RR 0.22; 95% CI 0.12–0.39; P < 0.00001) were significantly lower in FET. No significant differences were found for biochemical pregnancy, ongoing pregnancy, or implantation rates.	Low risk (NOS = 9/9). High-quality RCTs included; comprehensive search strategy; consistent effect estimates; low heterogeneity for major outcomes.
Coates et al., United States, 2017 [35]	Randomized controlled trial	1 year 8 months	Fresh ET (n= 88); Frozen ET (n= 91)	Implantation rate per embryo transferred was slightly higher in the frozen group compared with fresh ET (75% vs. 67%; not statistically significant). Ongoing pregnancy rate (80% vs. 61%) and live birth rate per ET (77% vs. 59%) were significantly higher in the frozen group.	Low risk (NOS = 9/9). Randomization performed, well-defined population, standardized outcome measures, minimal risk of bias.

5. Discussion

This systematic review offers an updated synthesis of current evidence comparing pregnancy and neonatal outcomes following conventional (fresh) and frozen embryo transfer (FET) in IVF/ICSI cycles. Overall, the findings suggest that fresh embryo transfer is more frequently associated with adverse perinatal outcomes, including preterm delivery, low birth weight (LBW), and small-for-gestational-age (SGA) neonates. In contrast, pregnancies achieved through frozen embryo transfer are more commonly characterized by increased birth weight, with higher rates of macrosomia and large-for-gestational-age (LGA) infants. Notably, across the included studies, no meaningful differences were observed between fresh ET and FET with respect to congenital malformations or neonatal mortality, indicating that the method of embryo transfer does not appear to influence the overall risk of congenital anomalies [11-16, 18-27].

The results of the present review align with prior research demonstrating that fresh embryo transfer cycles are often linked to restricted fetal growth and preterm birth, whereas frozen embryo transfer is generally associated with more favorable growth parameters at birth [14, 21, 24, 26, 36, 37]. Previous analyses by Roque et al. (2019) and Cavoretto et al. (2022) have similarly proposed that frozen embryo transfer may enhance endometrial receptivity and reduce embryonic exposure to the supraphysiologic hormonal environment induced by ovarian stimulation, thereby supporting improved fetal growth [33, 37]. Nonetheless, several studies have reported an increased prevalence of macrosomia and hypertensive disorders of pregnancy following FET, which may reflect augmented placental perfusion and compensatory fetal growth mechanisms [19, 38]. Importantly, these maternal complications were not accompanied by higher rates of perinatal death or congenital anomalies [15, 20, 23]. Collectively, evidence from diverse populations suggests a consistent pattern whereby FET reduces the risk of fetal growth restriction but may predispose to higher birth weight, particularly in cycles utilizing artificial endometrial preparation protocols.

The observed differences in outcomes between fresh and frozen embryo transfer are likely attributable to variations in the hormonal and endometrial milieu at the time of implantation. In fresh transfer cycles, elevated estrogen and progester-

one concentrations resulting from controlled ovarian stimulation may compromise endometrial receptivity and placental development, thereby increasing the risk of SGA and preterm birth [39, 40]. Conversely, frozen embryo transfer—especially when performed in a natural or hormonally balanced cycle—allows implantation to occur under conditions that more closely resemble normal physiology, which may promote optimal placentation and fetal growth [15, 22, 27]. However, emerging evidence indicates that certain artificial FET protocols involving hormone replacement therapy (HRT) and gonadotropin-releasing hormone (GnRH) agonist suppression may lead to excessive placental perfusion, contributing to higher rates of LGA and macrosomia observed in frozen cycles [13, 18, 21, 25]. Furthermore, Hwang et al. (2019) reported an increased incidence of respiratory and neurological complications among infants conceived via FET, potentially secondary to fetal overgrowth and associated delivery-related risks [15]. These findings underscore the complex interaction between hormonal exposure, implantation timing, and subsequent fetal development.

By incorporating data from a broad range of prospective and retrospective studies conducted across multiple geographic regions, this systematic review provides a comprehensive overview of perinatal outcomes associated with embryo transfer strategies in ART. Restricting inclusion to singleton pregnancies derived from autologous embryos reduced confounding related to multiple gestation and donor gamete use. Additionally, the inclusion of large-scale studies from Nordic, Asian, and European cohorts enhances the generalizability of the findings [14, 16, 18, 22]. Nevertheless, several limitations must be acknowledged. A substantial proportion of the included studies were observational in design, which introduces the potential for selection bias and residual confounding despite statistical adjustment.

6. Limitations of the Study

The present review has some limitations that are worth mentioning. A limited number of randomized controlled trials (RCTs) were available, and differences in clinical protocols, endometrial preparation methods, and embryo culture techniques may have contributed to heterogeneity in reported outcomes. Additionally, this review excluded non-English publications and unpublished data, which may introduce publication bias. Despite these limitations, the consistency of findings across diverse study designs and populations supports the reliability of the conclusion that FET improves fetal growth outcomes but may predispose to fetal overgrowth.

7. Conclusion

Based on the evidence synthesized in this systematic review, singleton pregnancies achieved through frozen embryo transfer (FET) demonstrate overall more favorable neonatal outcomes compared with those resulting from conventional fresh embryo transfer (ET) in IVF/ICSI cycles. Frozen embryo transfer is consistently associated with reduced risks of preterm birth, low birth weight, and small-for-gestational-age (SGA) infants, whereas fresh ET appears more frequently linked to fetal growth restriction and earlier gestational delivery. Importantly, no significant differences were identified between fresh and frozen transfer strategies with respect to congenital malformations or neonatal mortality, indicating comparable safety profiles for both approaches.

These findings support the concept that frozen embryo transfer may offer a more physiologic endometrial environment, facilitate improved implantation conditions and support optimal fetal growth and development. However, the relative advantages of each transfer strategy vary according to patient characteristics and clinical circumstances, underscoring the need for careful interpretation of outcomes within individualized treatment contexts.

8. Recommendations

Given the heterogeneous nature of IVF/ICSI populations, clinical decision-making regarding embryo transfer strategy should be individualized. Factors such as maternal age, underlying cause of infertility, ovarian response to stimulation, endometrial receptivity, and prior ART outcomes should be carefully considered when selecting between fresh and frozen embryo transfer. While FET offers clear advantages in terms of neonatal growth outcomes and maternal safety in selected patients, fresh ET may remain appropriate in specific clinical scenarios.

Further well-designed prospective studies are warranted to clarify the long-term health implications of embryo transfer type on offspring, including metabolic, cardiovascular, and neurodevelopmental outcomes. Future research should also focus on elucidating the biological mechanisms responsible for differences in fetal growth patterns, particularly the roles of endometrial preparation protocols, cryopreservation methods, and embryo thawing techniques. Continued refinement of cryotechnology, laboratory practices, and patient-centered treatment protocols will be essential to optimize the safety, efficacy, and personalization of embryo transfer strategies in modern reproductive medicine.

Abbreviations

AFC	Antral Follicle Count
AOR	Adjusted Odds Ratio
ART	Assisted Reproductive Technology
BMI	Body Mass Index
CI	Confidence Interval
CPR	Clinical Pregnancy Rate
DPI	Dry Powder Inhaler

ET	Embryo Transfer
FET	Frozen Embryo Transfer
FSH	Follicle-stimulating Hormone
GnRH	Gonadotropin-releasing Hormone
HRT	Hormone Replacement Therapy
ICSI	Intracytoplasmic Sperm Injection
IRR	Incidence Rate Ratio
IVF	In Vitro Fertilization
LBW	Low Birth Weight
LBR	Live Birth Rate
LGA	Large for Gestational Age
MeSH	Medical Subject Headings
NOS	Newcastle–Ottawa Scale
OHSS	Ovarian Hyperstimulation Syndrome
OR	Odds Ratio
PCOS	Polycystic Ovary Syndrome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomized Controlled Trial
RoB 2	Revised Cochrane Risk of Bias Tool (Version 2)
RR	Risk Ratio
R-ICSI	Rescue Intracytoplasmic Sperm Injection
SD	Standard Deviation
SGA	Small for Gestational Age

Conflicts of Interest

The authors declare no conflicts of interest.

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