INTRODUCTION

The realm of assisted reproductive technology has ushered in new opportunities for individuals and couples grappling with fertility challenges, with in vitro fertilization (IVF) standing at the forefront of these advancements. Within the intricate web of hormonal orchestration that underpins successful IVF outcomes, the roles of both estradiol (E2) and progesterone are pivotal. Estrogen, a fundamental player in follicular growth and endometrial preparation, joins forces with progesterone to create an environment conducive to embryo implantation and subsequent pregnancy. Among the various phases of IVF, the period of progesterone support stands as a critical juncture, encompassing the phase during which the embryo is expected to establish its foothold within the endometrium.

The administration of exogenous progesterone support during the luteal phase of IVF cycles aims to bridge the hormonal gap left by the absence of a corpus luteum, which would typically produce progesterone after ovulation. However, within this complex hormonal landscape, the role and interplay of estrogen levels on the day of progesterone support have garnered increasing attention. The extent to which E2 serum levels influence pregnancy outcomes, particularly during this crucial phase of progesterone supplementation, presents a captivating avenue for exploration. Previous studies have tried to explore the effect of estradiol serum level and pregnancy outcomes, however, the results are varied and inconclusive.

This systematic review embarks on a comprehensive journey to dissect the relationship between E2 serum levels on progesterone support day and pregnancy outcomes among IVF patients. By meticulously compiling and synthesizing a plethora of research studies, this investigation aims to unravel the nuanced interactions between E2 levels, progesterone supplementation, and pivotal IVF outcomes such as clinical pregnancy rates, implantation rates, miscarriage rates, and the overall trajectory towards a successful live birth. The synthesis of a diverse body of evidence holds the potential to provide a panoramic view of the intricate interplay between estrogen and progesterone dynamics, shedding light on the degree to which these hormones collaboratively influence...
the final chapter of the IVF journey.

As fertility science advances and precision medicine gains traction, understanding the impact of E2 serum levels on progesterone support day becomes paramount. By delving into this scientific frontier, we strive to offer practitioners and patients alike a comprehensive understanding of the role of estrogen in shaping the landscape of IVF success. Armed with these insights, clinicians can potentially fine-tune treatment strategies, personalize interventions, and ultimately enhance the prospects of realizing the cherished dream of parenthood for those navigating the path of assisted reproduction.

MATERIAL AND METHODS

Study Design and Selection Criteria

A systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies published up to August 2023 were searched using electronic databases including PubMed and Embase. The inclusion criteria comprised studies that investigated the relationship between serum estrogen (E2) levels on progesterone support day and pregnancy outcomes among in vitro fertilization (IVF) patients. Exclusion criteria include studies that involve fresh embryo transfers. Primary outcomes of interest included clinical pregnancy rates, implantation rates, miscarriage rates, and live birth rates. Only studies published in English were considered.

Data Collection and Extraction

Two independent reviewers screened the identified studies based on titles and abstracts for eligibility. Subsequently, full-text articles of potentially eligible studies were assessed for final inclusion. Discrepancies were resolved through discussion and consensus. Data extraction was performed using a standardized form, capturing study characteristics (author, year, design), patient demographics (sample size, age), hormonal protocols (progesterone regimen, E2 measurement), and outcomes (clinical pregnancy rate, implantation rate, miscarriage rate, live birth rate).

Quality Assessment

The quality and risk of bias of included studies were assessed using relevant tools, such as the Newcastle-Ottawa Scale (NOS) for observational studies. Studies were evaluated based on selection criteria, comparability of groups, and outcome assessment. The risk of publication bias was assessed using funnel plots and the Egger's test.

Data Synthesis and Statistical Analysis

Meta-analysis was performed using Review Manager version [insert version number]. Pooled risk ratios (RR) with 95% confidence intervals (CI) were calculated for the outcomes of interest. Heterogeneity among studies was assessed using the I-squared (I²) statistic. A fixed-effects model was employed for studies with minimal heterogeneity (I² < 50%), while a random-effects model was used for studies with substantial heterogeneity. Subgroup analyses were conducted when appropriate.

Sensitivity Analysis and Publication Bias

Sensitivity analysis was performed by excluding studies with a high risk of bias or those significantly deviating from the overall effect size. Publication bias was assessed using funnel plots and Egger’s test, with visual asymmetry indicating potential bias.

Ethical Considerations

As this study involved the analysis of previously published data, ethical approval was not required.
Data Availability
Data extracted from the included studies and relevant meta-analysis results are available upon request.

RESULTS

Study Selection Process
The study selection process involved a comprehensive search of databases, yielding an initial total of 159 articles from PubMed and 40 from Embase. After identifying and removing duplicate records, 35 duplicates were excluded. Subsequently, 4 articles were rendered inaccessible due to unavailable abstracts. Evaluation of the remaining articles against the predefined Population, Intervention, Comparison, and Outcome (PICO) criteria led to the exclusion of 149 studies that were deemed irrelevant to the research objectives. This screening process resulted in a final selection of 8 studies that met the inclusion criteria and were subsequently included for analysis.

The included studies span various years and encompass a diversity of methodologies, each offering unique insights into the relationship between serum estrogen levels and pregnancy outcomes in the context of IVF. In 2002, Banz et al.\(^5\) conducted a retrospective cohort study involving 52 control cycles with an estradiol threshold of \(<150\) pg/mL and 46 cycles with a threshold of \(>450\) pg/mL. The estradiol serum level on day 14 of the cycle was the focus, assessing its impact on live birth rates. Niu et al.\(^6\) in 2008 explored clinical pregnancy rates, miscarriage rates, and endometrial thickness with serum estradiol levels of \(110\) pg/mL as the threshold in 55 control cycles and 84 cycles/patients.

Moving forward, Fritz et al.\(^7\) delved into a cohort of 36 cycles in 2017, utilizing trough E2 levels that were measured twice weekly for at least 2 cycles and trough E2 dosage was adjusted accordingly to achieve levels of 200–500 pg/ml following 8–10 days of E2 supplementation. Their study focused on live birth rates. Mackens et al.\(^4\) (2020) conducted a large retrospective cohort study involving 124 cycles with a threshold of \(<145\) pg/mL for control cycles and 121 cycles/patients with a threshold of \(>439\) pg/mL. They measured serum E2 levels 1 or 2 days before initiating

### Table 1. Characteristics and Findings of Included Studies

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Type</th>
<th>Control Cycles</th>
<th>Threshold (pg/mL)</th>
<th>Comparator Cycles/ patients</th>
<th>Timing</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>Banz et al.(^5)</td>
<td>RCS</td>
<td>52</td>
<td>(&lt;150)</td>
<td>46</td>
<td>&gt;450</td>
<td>Estradiol serum level on day 14</td>
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<tr>
<td>2008</td>
<td>Niu et al.(^6)</td>
<td>RCS</td>
<td>55</td>
<td>110</td>
<td>84</td>
<td>&gt;299</td>
<td>Clinical pregnancy rate, miscarriage rates, endometrial thickness</td>
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<tr>
<td>2008</td>
<td>Niu et al.(^6)</td>
<td>RCS</td>
<td>55</td>
<td>110</td>
<td>84</td>
<td>&gt;299</td>
<td>Clinical pregnancy rate, miscarriage rates, endometrial thickness</td>
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<tr>
<td>2017</td>
<td>Fritz et al.(^7)</td>
<td>RCS</td>
<td>36</td>
<td>135</td>
<td>74</td>
<td>&gt;692</td>
<td>Estradiol levels measured twice weekly for at least 2 cycles</td>
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<td>2017</td>
<td>Fritz et al.(^7)</td>
<td>RCS</td>
<td>36</td>
<td>135</td>
<td>74</td>
<td>&gt;692</td>
<td>Estradiol levels measured twice weekly for at least 2 cycles</td>
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<td>2020</td>
<td>Mackens et al.(^4)</td>
<td>RCS</td>
<td>124</td>
<td>135</td>
<td>74</td>
<td>&gt;692</td>
<td>Estradiol levels measured twice weekly for at least 2 cycles</td>
</tr>
<tr>
<td>2020</td>
<td>Mackens et al.(^4)</td>
<td>Large RCS</td>
<td>124</td>
<td>135</td>
<td>74</td>
<td>&gt;692</td>
<td>Estradiol levels measured twice weekly for at least 2 cycles</td>
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<tr>
<td>2021</td>
<td>Beck-Fruchter et al.(^8)</td>
<td>RCS</td>
<td>230</td>
<td>188.2</td>
<td>230</td>
<td>364</td>
<td>Estradiol levels measured 14 days after FET using commercially available kit</td>
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<tr>
<td>2021</td>
<td>Zhang et al.(^9)</td>
<td>RCS</td>
<td>22</td>
<td>22</td>
<td>&gt;91.16</td>
<td>195</td>
<td>Serum E2 levels measured 14 days after FET using commercially available kit</td>
</tr>
<tr>
<td>2021</td>
<td>Zhou et al.(^10)</td>
<td>RCS</td>
<td>1676</td>
<td>&lt;200</td>
<td>&gt;400</td>
<td>885</td>
<td>Serum E2 levels measured 14 days after FET using commercially available kit</td>
</tr>
<tr>
<td>2022</td>
<td>Goldman et al.(^11)</td>
<td>RCS</td>
<td>90</td>
<td>212</td>
<td>528</td>
<td>90</td>
<td>Serum E2 levels measured 14 days after FET using commercially available kit</td>
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</tbody>
</table>

progesterone supplementation for luteal phase induction. Live birth rates and endometrial thickness were their main outcomes.

In 2021, Beck-Fruchter et al. observed a cohort of 230 cycles and assessed estradiol levels 14 days post frozen embryo transfer (FET) using commercially available kits, linking them to live birth rates, clinical pregnancy rates, miscarriage rates, implantation rates, and biochemical rates. Zhang et al. that same year studied

### Table 2. Risk of bias assessment of cohort studies using NOS

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<td>Ascertainment of exposure (1)</td>
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<tr>
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<td>2</td>
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<td>Outcome</td>
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<td>Assessment of outcome (1)</td>
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<td>Was follow-up long enough for outcomes to occur? (1)</td>
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<td>Adequacy of follow-up of cohorts (1)</td>
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**Figure 2.** Forest plot of the comparison of estradiol level on live birth rate.

**Figure 3.** Forest plot of the comparison of estradiol level on live birth rate considering the day of progesterone.
examined 1676 cycles in 2021, evaluating live birth rates, clinical pregnancy rates, miscarriage rates, and biochemical rates. They associated serum estradiol levels of <200 pg/mL and >400 pg/mL with the day of progesterone injection. Lastly, Goldman et al.\textsuperscript{11} in 2022 engaged in 90 cycles, analyzing live birth rates, clinical pregnancy rates, miscarriage rates, implantation rates, and endometrial thickness in response to serum estradiol levels of 212 pg/mL as the threshold, specifically on the day of progesterone start.

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**Figure 4.** Forest plot of the comparison of estradiol level on implantation rate.

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**Figure 5.** Forest plot of the comparison of estradiol level on implantation rate upon the exclusion of the Bech-Fruchter study.

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**Figure 6.** Forest plot of the comparison of estradiol level on miscarriage rate.

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**Figure 7.** Forest plot of the comparison of estradiol level on miscarriage rate upon Excluding the Zhang et al. study.
Risk of Bias assessment

The risk of bias assessment for cohort studies, utilizing the Newcastle-Ottawa Scale (NOS), is presented in Table 2. Adopting a cut-off score of 6, all studies demonstrated a low risk of bias.

Live Birth Rate

Live birth rates were assessed across 7 distinct studies in this analysis. The calculated risk ratio (RR) stood at 1.34 (95% confidence interval [CI] 0.85-2.11), with a p-value of 0.21. A notable level of heterogeneity was observed within the group, with an I-square value of 90%. This heterogeneity is likely due to intrinsic differences among the included studies. Importantly, the exposed group, characterized by elevated estradiol levels, demonstrated a propensity for heightened live birth rates, whereas the control group exhibited lower estradiol levels and relatively reduced outcomes. A cumulative total of 1677 events were documented in the experimental group, whereas the control group consisted of 2304 events. Despite the non-significant risk ratio, indicating that a conclusive link between elevated estradiol levels and increased live birth rates couldn't be established within this dataset, these findings underscore the need for further exploration. Additionally, considering the substantial inter-study heterogeneity, the interpretation of the intricate interplay between estradiol levels and live birth rates warrants careful consideration.

Conducting a subgroup analysis exclusively considering the day of the progesterone trigger led to a reduction in heterogeneity, although moderate variance persisted. Investigating the live birth rate across three studies, the recalculated risk ratio (RR) emerged as 0.80 (95% confidence interval [CI] 0.66-0.97), accompanied by a p-value of 0.02. Notably, within-group heterogeneity was mitigated to a degree, with an I-square value of 41%. This residual variance suggests that despite the subgroup focus, certain differences between the studies persist. Significantly, the experimental group, marked by elevated estradiol levels, exhibited a distinct inclination towards diminished live birth rates. In contrast, the control group, characterized by lower estradiol levels, demonstrated relatively heightened outcomes. The cumulative event count within the experimental group amounted to 1096, while the control group encompassed 1890 events. The recalculated risk ratio underscores a notable significance; however, the
continued presence of moderate heterogeneity emphasizes the nuanced nature of the relationship between estradiol levels and live birth rates. These findings highlight the importance of comprehensive investigation and the consideration of potential factors contributing to the remaining variance within this refined subgroup analysis.

**Implantation Rate**

Examining the implantation rate across three distinct studies, the calculated risk ratio (RR) emerged as 1.02 (95% confidence interval [CI] 0.53-1.95), with a p-value of 0.96. Notably, within-group heterogeneity was significant, marked by an I-square value of 83%. This substantial variance is likely attributed to inherent differences among the studies. Pertinently, the exposed group, characterized by heightened estradiol levels, demonstrated a propensity for a slightly elevated implantation rate, while the control group exhibited lower estradiol levels and comparatively diminished outcomes. The cumulative event count in the experimental group reached 404, whereas the control group accounted for 375 events. Despite the non-significant risk ratio, which implies that a definitive connection between higher estradiol levels and increased implantation rates couldn't be established within this dataset, these findings highlight the need for further exploration. Additionally, given the pronounced inter-study heterogeneity, a nuanced understanding of the complex interplay between estradiol levels and implantation rates is imperative. Higher estradiol has a higher implantation rate than the lower group, but the results are not significant. Heterogeneity is substantial.

Upon the exclusion of the Bech-Fruchter study, a notable reduction in heterogeneity to 0% was observed, a significant development considering the previous variability attributed to the unique timing of estradiol level measurement in that study. Worth noting is that, interestingly, the higher estradiol group exhibited a significantly lower implantation rate. In this refined context, analyzing implantation rates across two studies, the recalculated risk ratio (RR) stood at 0.69 (95% confidence interval [CI] 0.54-0.88), with a p-value of 0.003. Remarkably, within-group heterogeneity reached a negligible 0%, an outcome that aligns with the homogeneity achieved upon the study's exclusion. Reiterating, the experimental group featuring elevated estradiol levels demonstrated a distinct inclination towards reduced implantation rates, while the control group, characterized by comparatively lower estradiol levels, exhibited relatively higher outcomes. The combined event tally within the experimental group comprised 174 instances, while the control group accounted for 145 events. These findings, despite the pronounced significance of the recalculated risk ratio, warrant further exploration. Given the observed interplay between estradiol levels and implantation rates and the mitigated heterogeneity in this refined analysis, a meticulous understanding of the intricate dynamics within this context is crucial.

**Miscarriage Rate**

An intriguing observation emerges as the data suggests that the higher estradiol group exhibits a lower miscarriage rate in comparison to the lower estradiol group, although this difference does not reach statistical significance. The analysis of miscarriage rates across five studies yields a recalculated risk ratio (RR) of 0.84 (95% confidence interval [CI] 0.51-1.41), with a p-value of 0.52. Remarkably, within-group heterogeneity remains at a moderate level, as indicated by an I-square value of 57%. This persistent variance underlines that despite trends toward reduced miscarriage rates, certain differences between the studies continue to influence the results. Notably, the experimental group characterized by elevated estradiol levels displayed a tendency towards fewer miscarriages, while the control group, characterized by lower estradiol levels, experienced relatively fewer instances. Within this refined context, the cumulative event count within the experimental group totaled 1305, while the control group comprised 1525 occurrences. Although the recalculated risk ratio approaches unity and the p-value remains non-significant, the reduced heterogeneity following the removal of the Zhang et al. study warrants attention. The influence of aromatase inhibitors on the relationship between estradiol levels and miscarriage rates underscores the importance of tailored subgroup analysis and elucidates potential nuances within this intricate interplay.

**Clinical Pregnancy Rates**

The analysis of clinical pregnancy rates across five studies suggests a trend wherein the higher estradiol group demonstrates a relatively higher clinical pregnancy rate compared to the lower estradiol group, though this difference does not attain statistical significance. The recalculated risk ratio (RR) is recorded as 1.02 (95% confidence interval [CI] 0.79-1.31), accompanied by a p-value of 0.87. Notably, within-group heterogeneity persists at a
substantial level, indicated by an I-square value of 78%. Even after employing leave-one-out meta-analysis to ascertain potential sources of heterogeneity, the variance remains pronounced, underscoring the complex nature of the relationship. The experimental group characterized by heightened estradiol levels showcases a marginal inclination toward enhanced clinical pregnancy rates, while the control group, marked by lower estradiol levels, experiences comparatively lower rates. The cumulative event count within the experimental group amounts to 1484 instances, with the control group reporting 2073 occurrences. Despite the non-significant risk ratio and the sustained substantial heterogeneity, these findings suggest a potential trend worthy of further exploration. The lack of homogeneity even in leave-one-out analyses emphasizes the intricate interplay between estradiol levels and clinical pregnancy rates, urging for a comprehensive understanding and meticulous consideration of contributing factors across the studies.

**Endometrial Thickness**

The investigation into endometrial thickness across five studies yielded no significant disparity between groups characterized by higher or lower estradiol levels. The calculated mean difference is recorded at a mere -0.01 (95% confidence interval [CI] -0.35, 0.33), accompanied by a p-value of 0.96. Notably, the heterogeneity within the group remains substantial, denoted by an I-square value of 92%. The attempt to mitigate this variance through leave-one-out meta-analysis proved futile, signifying the persistent complexity of the relationship. Despite the non-significant mean difference, the experimental group marked by elevated estradiol levels demonstrated a marginal trend towards slightly reduced endometrial thickness, while the control group, characterized by lower estradiol levels, displayed a modest inclination towards thicker endometrial linings. The cumulative event count within the experimental group stands at 1375 instances, with the control group reporting 1967 occurrences. The lack of significant findings combined with substantial heterogeneity and unsuccessful heterogeneity reduction attempts emphasizes the intricate interplay between estradiol levels and endometrial thickness. This underscores the importance of considering multifaceted variables contributing to the observed variance across the studies.

**Biochemical Pregnancy**

The analysis of biochemical pregnancy rates across three studies reveals a notable pattern wherein the higher estradiol group exhibits a significantly lower biochemical pregnancy rate in contrast to the lower estradiol group. The recalculated risk ratio (RR) emerges as 0.94 (95% confidence interval [CI] 0.90-0.99), accompanied by a p-value of 0.02. Remarkably, the heterogeneity within this group is negligible, indicated by an I-square value of 0%, which underscores a high level of homogeneity in the dataset. The experimental group, characterized by elevated estradiol levels, demonstrates a pronounced tendency towards fewer biochemical pregnancies, while the control group with lower estradiol levels experiences comparatively more instances. Within this context, the cumulative event count within the experimental group comprises 1198 occurrences, while the control group tallies 2004 instances. The significant risk ratio coupled with minimal heterogeneity emphasizes the robustness of the observed trend. These findings offer valuable insights into the potential influence of estradiol levels on biochemical pregnancy rates, suggesting a noteworthy association worthy of further exploration and consideration of underlying mechanisms across the studies.

**DISCUSSION**

The systematic review and meta-analysis conducted in this study aimed to explore the relationship between serum estradiol levels on various trigger days and their potential impact on pregnancy outcomes among in vitro fertilization (IVF) patients. The findings across different outcome measures provide valuable insights into the intricate interplay between estradiol levels and IVF success.

The investigation into live birth rates revealed a trend suggesting that higher estradiol levels might be associated with an elevated live birth rate. However, this association did not reach statistical significance, indicating the need for caution in drawing definitive conclusions. The analysis presented a risk ratio of 1.34, with a 95% confidence interval of 0.85-2.11 and a p-value of 0.21. The substantial heterogeneity observed (90%) underscores the challenges of elucidating a consistent relationship between estradiol levels and live birth outcomes.

Implantation rates, crucial indicators of successful embryo attachment, exhibited a non-significant risk ratio of 1.02 (95% CI 0.53-1.95) with a p-value of 0.96. This suggests that while higher estradiol levels might be associated with a marginal increase in implantation rates, the observed effect lacks statistical significance. The substantial within-group heterogeneity (83%) complicates interpretation, indicating diverse impacts across different studies.

Interestingly, the analysis of miscarriage rates suggested that higher estradiol levels might be associated with a marginally lower risk of miscarriage. However, similar to other outcome measures, this association did not reach statistical significance, as indicated by the risk ratio of 0.84 (95% CI 0.51-1.41) and a p-value of 0.52. The moderate within-group heterogeneity (57%) further emphasizes the complex nature of this relationship.

The investigation into clinical pregnancy rates revealed a trend suggesting that higher estradiol levels might lead to slightly higher clinical pregnancy rates. However, similar to other outcome measures, this trend did not attain statistical significance, as indicated by the risk ratio of 1.02 (95% CI 0.79-1.31) and a p-value of 0.87. The substantial within-group heterogeneity (78%) highlights the variability in reported effects across studies.

Endometrial thickness, another pivotal factor in IVF success, showed no significant difference between higher and lower estradiol groups. The analysis yielded a mean difference of -0.01 (95% CI -0.35, 0.33) with a p-value of 0.96, suggesting that estradiol levels might not strongly influence endometrial thickness. The high within-group heterogeneity (92%) points to the complexity of this relationship.
Notably, the analysis of biochemical pregnancy rates revealed a significant association between higher estradiol levels and a lower risk of biochemical pregnancies. The risk ratio was 0.94 (95% CI 0.90-0.99) with a p-value of 0.02, suggesting a potentially protective effect of higher estradiol levels against biochemical pregnancy. The negligible within-group heterogeneity (0%) enhances the robustness of this finding.

This systematic review and meta-analysis offer a thorough examination of the intricate relationship between serum estradiol levels on different trigger days and their potential impact on diverse pregnancy outcomes in the context of in vitro fertilization (IVF). In fresh cycles, excessive estradiol (E2) levels have been demonstrated to hurt endometrial growth and, consequently, can hinder successful conception. Furthermore, elevated E2 levels have been associated with a higher occurrence of pregnancy-related complications like intrauterine growth restriction and irregular placental implantation. Therefore, it can be expected to happen the same in frozen embryo transfers. However, there are still only a limited number of studies conducted to explain the nature of the molecular relationship between estradiol serum level and pregnancy outcomes in frozen embryo transfer in IVF. Our study applied inclusion criteria of a range of studies across various trigger timings strengthening the comprehensive nature of this analysis, and providing a broader understanding of the topic. The study's scope encompasses critical IVF outcomes, including live birth rates, implantation rates, miscarriage rates, clinical pregnancy rates, endometrial thickness, and biochemical pregnancy rates.

Nonetheless, the review is not without limitations. The substantial heterogeneity observed within several outcome measures could potentially be attributed to variations in study designs, patient populations, and methodologies. The diversity in estradiol thresholds for classifying higher and lower groups across different studies might introduce bias, impacting the overall findings. Despite these challenges, this review underscores the importance of addressing the multifaceted nature of estradiol's influence on IVF outcomes, as evidenced by the complex interactions and the lack of consistent patterns observed in the results.

To strengthen the reliability and generalizability of future investigations in this domain, it is recommended to adopt standardized methodologies and protocols for measuring estradiol levels and categorizing patient groups based on these levels. Larger sample sizes and more extensive datasets would contribute to more robust conclusions. Moreover, the implementation of prospective studies that rigorously control for potential confounding factors, such as patient characteristics and treatment protocols, could shed further light on the nuanced relationships between estradiol levels and IVF outcomes. Additionally, exploring potential mechanisms underlying the associations observed could provide valuable insights into the biological processes at play. In conclusion, while this review expands our understanding of the topic, future research endeavors should aim for greater methodological consistency and depth of analysis to unravel the complexities of estradiol's impact on IVF success comprehensively.

CONCLUSION

In conclusion, this systematic review and meta-analysis offer a comprehensive evaluation of the intricate interplay between serum estradiol levels on various trigger days and their potential effects on a spectrum of IVF outcomes. The findings highlight the complexity of the relationship, with varying degrees of impact observed across different outcomes and trigger timings. While certain trends emerge, the heterogeneity among studies underscores the need for more standardized methodologies and larger, well-controlled prospective studies to elucidate the nuanced associations between estradiol levels and IVF success. This analysis contributes to our understanding of the role of estradiol in IVF outcomes, paving the way for further research to unravel the multifaceted mechanisms at play and ultimately optimize fertility treatment protocols.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FUNDINGS

This review is not funded by any organization, institution, or other third parties.

ETHICAL STATEMENT

Not applicable.

AUTHOR CONTRIBUTION

All authors contributed equally to this study.

REFERENCES


