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Letter to Editor

Critical appraisal on spontaneous pregnancy following intra-ovarian platelet-rich plasma administration in poor ovarian responders according to the POSEIDON criteria

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Dear Editor

The study by Sanuie Farimani et al. (1) evaluating spontaneous pregnancy after intra-ovarian platelet-rich plasma (IO-PRP) administration in women with poor ovarian response (POR) according to the POSEIDON criteria addresses an important problem in assisted reproduction. The use of POSEIDON for finer prognostic stratification is appropriate and strengthens clinical interpretation (2). The initial cohort of 1548 women and the 2-yr follow-up demonstrate notable effort, and the report of 42 spontaneous pregnancies provides useful descriptive data in this emerging field.

However, several limitations temper the study's conclusions. The retrospective cross-sectional design without a control arm precludes causal inference: the observed 8.39% spontaneous pregnancy rate cannot be confidently attributed to PRP, given natural variability in POR outcomes and absence of comparator data. High attrition (≈61.5% lost to follow-up) raises further concern for selection bias, since those retained may not represent the original cohort. Comparable observational work has reported spontaneous conception rates of roughly 4–7% after PRP, suggesting the present rate may lie within expected background variation rather than indicating a robust treatment effect (3).

The clinical relevance of a modest spontaneous pregnancy rate in POR is also questionable. For patients of advanced reproductive age or with diminished ovarian reserve, delaying established assisted reproductive technologies in favor of an experimental intervention may reduce their cumulative likelihood of achieving a live birth. Although recent systematic reviews and meta-analyses suggest that PRP may improve surrogate markers such as anti-Müllerian hormone and antral follicle count and may increase oocyte/embryo yield (4, 5). A recent trial reported improved blastocyst yield and quality after IO-PRP, translation into consistent increases in live birth remains unproven (6).

Statistical issues further limit inference. Multiple subgroup comparisons across POSEIDON categories appear to have been performed without clear correction for multiple testing, increasing the risk of type I error. Associations reported with age, anti-Müllerian hormone, body mass index, and follicle counts may therefore reflect chance findings. Important confounders including concurrent treatments, lifestyle factors, and partner fertility parameters were not comprehensively controlled, despite their potential impact on spontaneous conception (3–5).

Finally, heterogeneity in PRP preparation and administration across studies (centrifugation protocols, platelet concentration, injection volume, timing) complicates reproducibility and comparison. Even meta-analyses emphasize that outcome variability may be more related to methodological differences than to intrinsic efficacy (4, 5). Mechanistic understanding of how IO-PRP might restore or augment ovarian function remains incomplete, though recent clinical findings showing improved blastocyst quality suggest a potential biological role (6).

In summary, while Sanuie Farimani et al. contribute valuable observational data suggesting spontaneous pregnancy is possible after IO-PRP in a subset of POR patients, modest rates, high attrition, lack of a comparator arm, and statistical limitations warrant cautious interpretation. Well-designed randomized controlled trials with standardized PRP protocols and live birth as the primary endpoint are essential before IO-PRP can be recommended outside investigational settings.

Conflict of Interest

The author declares that there is no conflict of interest.

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