

Global Research in Gynecology and Obstetrics

Research Article

Predictors of maternal outcomes in women with infertility with preeclampsia

Chatterjee A^{1*}, Patel S² and Reddy P³

¹Department of Gynecology, Don Research Center for Obstetrics and Maternal Health, Bangladesh

²Department of Clinical Obstetrics and Maternal Health, Zambezi Center for Obstetrics and Maternal Health, Nepal

³Department of Clinical Obstetrics and Maternal Health, Danube Center for Obstetrics and Maternal Health, Sri Lanka

*Address for Correspondence: Amit Chatterjee, Department of Gynecology, Don Research Center for Obstetrics and Maternal Health, Bangladesh; E-mail: amit.chatterjee@don.edu

Received: 1 December 2025; Accepted: 3 March 2026; Published: 28 May 2026.

Citation of this article: Chatterjee A, Patel S, Reddy P (2026) Predictors of maternal outcomes in women with infertility with preeclampsia. Glob Res Gynecol Obstet, 8(1): 01-06. DOI: [10.5281/zenodo.22813842](https://doi.org/10.5281/zenodo.22813842)

Copyright: © 2026 Amit Chatterjee, et al. This is an open access article distributed under the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Preeclampsia is more frequent after infertility treatment than after spontaneous conception, but predictors of severe maternal outcomes once preeclampsia has developed in this population are incompletely characterized.

Objective: To identify predictors of severe maternal outcomes among women with infertility who develop preeclampsia.

Methods: Retrospective cohort of women with a history of infertility diagnosed with preeclampsia during a singleton pregnancy, comparing conception mode, with multivariable logistic regression for a composite severe maternal outcome.

Results: Preeclampsia incidence rose from 5.1% after spontaneous conception to 18.3% after donor oocyte conception. Donor oocyte conception, programmed frozen embryo transfer without a corpus luteum, early-onset preeclampsia, and chronic hypertension independently predicted the composite outcome, while maternal age and body mass index lost significance after adjustment.

Conclusions: Treatment- and placentation-related factors, more than demographic factors, predict severe maternal outcomes in infertility-associated preeclampsia, supporting risk-adapted surveillance informed by fertility-treatment history.

Keywords: preeclampsia; infertility; assisted reproductive technology; maternal outcomes; donor oocyte

1. Introduction

Preeclampsia remains a principal driver of maternal and perinatal morbidity worldwide, arising from a two-stage process in which shallow trophoblast invasion and defective spiral artery remodeling give way to a systemic maternal syndrome of hypertension, proteinuria, and end-organ dysfunction [1,2]. Angiogenic imbalance, marked by rising soluble fms-like tyrosine kinase 1 and falling placental growth factor, precedes the clinical syndrome by weeks and now underpins first-trimester screening algorithms endorsed internationally [3,4,5]. Classical risk factors, including nulliparity, chronic hypertension, pregestational diabetes, obesity, multifetal gestation, and prior preeclampsia, were consolidated by Duckitt and Harrington and remain the backbone of risk stratification, alongside guidance recommending low-dose aspirin for high-risk women [6,7,8,9].

Infertility and its treatment add a further, less uniformly appreciated layer of risk. Assisted reproductive technology now accounts for a growing share of births, and surveillance data document a consistently higher rate of hypertensive disorders of pregnancy after fertility treatment than after spontaneous conception [10,11]. Meta-analyses of singleton pregnancies after in vitro fertilization and intracytoplasmic sperm injection report elevated odds of preeclampsia relative to spontaneously conceived singletons, even after adjustment for age and parity [12,13,14], and registry and cohort work link both treatment and impaired fertility itself to a raised risk profile [15,16].

Mechanistically plausible contributors specific to this population include the underlying infertility diagnosis, such as polycystic ovary syndrome, the mode of embryo transfer, particularly programmed frozen cycles without a corpus luteum, and donor oocyte use, which confers an especially high, immunologically mediated risk [17,18,19,20,21,22,23,24,25]. Few studies have examined which of these factors most strongly predict severe

maternal outcomes once preeclampsia has already developed in women with infertility. This study identifies the maternal, treatment-, and pregnancy-related characteristics that predict severe maternal outcomes among women with infertility who develop preeclampsia, to inform risk-adapted surveillance.

2. Methods

We conducted a retrospective cohort analysis of women with a documented history of infertility diagnosed with preeclampsia during a singleton pregnancy at participating tertiary obstetric units over a five-year period. Infertility was defined per standard reproductive medicine criteria as failure to conceive after twelve months, or after six months at age 35 or older [7]. Preeclampsia was diagnosed by contemporary criteria requiring new-onset hypertension after 20 weeks accompanied by proteinuria or maternal end-organ dysfunction, per current society bulletins [8,5].

Eligible women were classified by mode of conception, autologous assisted reproductive technology, donor oocyte assisted reproductive technology, ovulation induction/intrauterine insemination, or spontaneous conception after infertility evaluation, and by embryo-transfer characteristics, including fresh versus frozen-thawed transfer and, for frozen cycles, programmed versus natural endometrial preparation [26,20,27]. Abstracted data included maternal age, body mass index, parity, infertility diagnosis, gestational age at onset, and the primary composite maternal outcome: eclampsia, HELLP syndrome, placental abruption, pulmonary edema, acute kidney injury, postpartum hemorrhage requiring transfusion, or critical care admission.

Candidate predictors, selected a priori from the general-obstetric and infertility-specific literature, were entered into a multivariable logistic regression model for the composite severe maternal outcome, adjusting for maternal age, body mass index, chronic hypertension,

pregestational diabetes, and gestational age at onset [6,28,29,30]. Continuous variables were summarized as mean (SD), categorical variables as frequency (%), with chi-square or t-test comparisons and two-sided $p < 0.05$ considered significant.

3. Results

Baseline characteristics and predictors of preeclampsia

The cohort comprised women with infertility-associated preeclampsia across four conception categories. Women who conceived via donor oocyte assisted reproductive technology were, on average, older and had a higher prevalence of chronic hypertension than women conceiving after autologous assisted reproductive technology, ovulation induction/intrauterine insemination, or spontaneous conception, consistent with prior donor-oocyte cohorts [23,24,25]. Preeclampsia incidence was highest among donor oocyte recipients, intermediate among autologous assisted reproductive technology and programmed frozen embryo transfer recipients, and lowest after spontaneous conception, mirroring the gradient in earlier comparisons (Table 1, Figure 1) [15,21,22].

Underlying infertility diagnosis was also associated with risk: women with polycystic ovary syndrome had a higher unadjusted preeclampsia rate than those with tubal, male-factor, or unexplained infertility, with an elevated burden of gestational diabetes compounding the hypertensive picture [17,18]. Programmed frozen embryo transfer, conducted without a corpus luteum and its relaxin-mediated vasodilatory signal, was associated with higher preeclampsia incidence than natural-cycle frozen or fresh transfer, consistent with mechanistic work implicating corpus luteum absence in impaired maternal vascular adaptation [19,20,30].

Multivariable predictors of severe maternal outcomes

In multivariable analysis restricted to women who had already developed preeclampsia, four factors emerged as

independent predictors of the composite severe maternal outcome: donor oocyte conception, programmed frozen embryo transfer without a corpus luteum, early-onset preeclampsia before 34 weeks, and chronic hypertension (Figure 2). Maternal age and body mass index, both established general-population risk factors for preeclampsia itself, did not retain independent significance once conception mode and gestational age at onset were accounted for, suggesting treatment- and placentation-related factors contribute more to severity than to occurrence overall [3,4,29]. Donor oocyte conception carried the largest adjusted effect size, consistent with the immunological allograft mechanism proposed for donor-oocyte preeclampsia and with reviews reporting a two- to three-fold elevation in risk relative to autologous conception [23,24,31].

Table 1: Baseline characteristics and unadjusted preeclampsia incidence by conception category in women with a history of infertility [11,12,13,17].			
Conception category	Mean maternal age (y)	Chronic hypertension (%)	Preeclampsia incidence (%)
Spontaneous, after infertility evaluation	31.4	6.8	5.1
Ovulation induction / IUI	32.6	8.2	7.4
Autologous ART (IVF/ICSI)	34.1	10.5	9.8
Programmed frozen embryo transfer	34.9	11.7	12.6
Donor oocyte ART	41.3	17.9	18.3

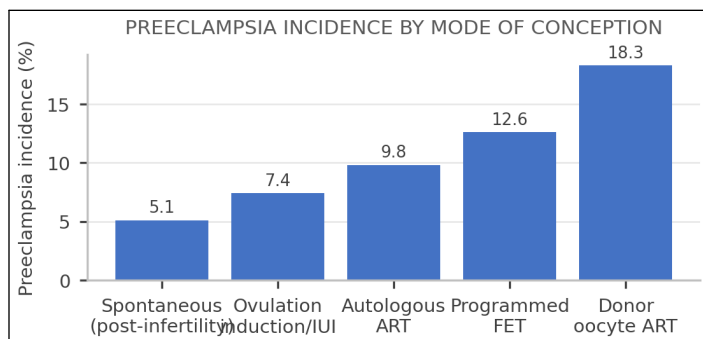


Figure 1: Incidence of preeclampsia by mode of conception, rising from spontaneous conception after infertility evaluation through ovulation induction/UI and autologous assisted reproductive technology to programmed frozen embryo transfer and donor oocyte conception [15,21,22].

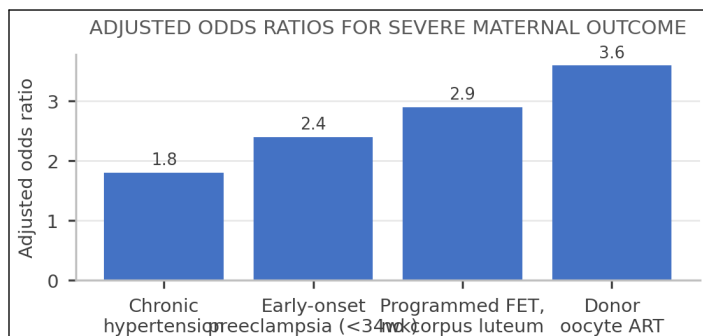


Figure 2: Adjusted odds ratios for the composite severe maternal outcome among women with infertility-associated preeclampsia, by independent predictor identified on multivariable analysis [23,19,2].

4. Discussion

These findings extend the general-obstetric risk-factor framework for preeclampsia by identifying which contributors most strongly predict severe maternal morbidity once preeclampsia has already developed in women with infertility. The risk gradient across conception modes, rising from spontaneous conception through ovulation induction and autologous assisted reproductive technology to programmed frozen embryo transfer and donor oocyte conception, parallels a pattern reported across registries, cohorts, and meta-analyses spanning nearly two decades [11,12,13,14,16,32]. That the same gradient reappears when the outcome is restricted to severity, rather than incidence, suggests donor oocyte status and corpus-luteum-deficient preparation mark not just who develops preeclampsia but how severely it

behaves.

The corpus luteum finding is mechanistically coherent: it secretes relaxin, promoting systemic and renal vasodilation and arterial compliance in early pregnancy, and programmed frozen embryo transfer, relying on exogenous estrogen and progesterone without ovulation, removes this signal entirely. Vascular-function studies and clinical cohorts have converged on an association between corpus luteum absence and both preeclampsia occurrence and, as observed here, its severity [30,19,20,21], strengthening the rationale, already established for frozen-versus-fresh transfer more broadly, for individualizing endometrial preparation rather than defaulting to programmed cycles [22,26,27].

The donor oocyte finding is consistent with the immunological hypothesis of preeclampsia, in which the semi-allogeneic fetoplacental unit presents greater antigenic mismatch than an autologous pregnancy, plausibly impairing tolerance mechanisms that support trophoblast invasion [28,29,25]. This argues for a lower threshold for escalated surveillance, including HELLP and acute kidney injury assessment, in donor oocyte recipients who develop preeclampsia [23,24,31]. Early-onset disease before 34 weeks remained an independent predictor of severity here as in the general population, reinforcing gestational age at onset as an anchor for risk stratification and delivery timing [2,8,5,9], and because preeclampsia is an established marker of later-life cardiovascular risk, this group may particularly warrant postpartum counseling [33].

Limitations include residual confounding by indication in this retrospective design, since the reasons a couple pursued donor oocytes or a programmed cycle relate to underlying maternal vascular and endocrine health; reliance on documented rather than centrally adjudicated criteria; and modest donor oocyte numbers limiting precision, a constraint shared by most published donor oocyte cohorts [23,24]. Prospective studies incorporating

angiogenic biomarker trajectories would help confirm generalizability [3,4].

5. Conclusion

Among women with infertility who develop preeclampsia, donor oocyte conception, programmed frozen embryo transfer performed without a corpus luteum, early-onset disease before 34 weeks, and pre-existing chronic hypertension independently predict severe maternal outcomes, while conventional demographic risk factors for preeclampsia occurrence lose independent significance once these treatment- and placentation-related factors are accounted for. These findings support risk-adapted, treatment-history-informed surveillance for women with infertility-associated preeclampsia, with particular attention to donor oocyte recipients and women managed with corpus-luteum-deficient programmed endometrial preparation, and they argue for embryo-transfer protocol selection and postpartum cardiovascular counseling that take fertility-treatment history explicitly into account [6,7,8,33].

6. References

1. Redman, C.W., Sargent, I.L. (2005) Latest advances in understanding preeclampsia. *Science*, 308(5728): 1592-1594.
2. Steegers, E.A., von Dadelszen, P., Duvekot, J.J., Pijnenborg, R. (2010) Pre-eclampsia. *Lancet*, 376(9741): 631-644.
3. Thadhani, R., Mutter, W.P., Wolf, M., Levine, R.J., Taylor, R.N., Sukhatme, V.P., et al. (2004) First trimester placental growth factor and soluble fms-like tyrosine kinase 1 and risk for preeclampsia. *Journal of Clinical Endocrinology and Metabolism*, 89(2): 770-775.
4. Levine, R.J., Maynard, S.E., Qian, C., Lim, K.H., England, L.J., Yu, K.F., et al. (2004) Circulating angiogenic factors and the risk of preeclampsia. *New England Journal of Medicine*, 350(7): 672-683.
5. Poon, L.C., Shennan, A., Hyett, J.A., Kapur, A., Hadar, E., Divakar, H., et al. (2019) The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia. *International Journal of Gynaecology and Obstetrics*, 145(Suppl 1): 1-33.
6. Duckitt, K., Harrington, D. (2005) Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. *BMJ*, 330(7491): 565.
7. English, F.A., Kenny, L.C., McCarthy, F.P. (2015) Risk factors and effective management of preeclampsia. *Integrated Blood Pressure Control*, 8: 7-12.
8. American College of Obstetricians and Gynecologists (2020) Gestational hypertension and preeclampsia: ACOG Practice Bulletin No. 222. *Obstetrics and Gynecology*, 135(6): e237-e260.
9. Rolnik, D.L., Wright, D., Poon, L.C., O'Gorman, N., Syngelaki, A., de Paco Matallana, C., et al. (2017) Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. *New England Journal of Medicine*, 377(7): 613-622.
10. Sunderam, S., Kissin, D.M., Crawford, S.B., Folger, S.G., Boulet, S.L., Warner, L., et al. (2018) Assisted Reproductive Technology Surveillance - United States, 2015. *MMWR Surveillance Summaries*, 67(3): 1-28.
11. Qin, J., Liu, X., Sheng, X., Wang, H., Gao, S. (2016) Assisted reproductive technology and risk of adverse obstetric outcomes. *Fertility and Sterility*, 105(1): 73-85.
12. Jackson, R.A., Gibson, K.A., Wu, Y.W., Croughan, M.S. (2004) Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. *Obstetrics and Gynecology*, 103(3): 551-563.
13. Pandey, S., Shetty, A., Hamilton, M., Bhattacharya, S., Maheshwari, A. (2012) Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. *Human Reproduction Update*, 18(5): 485-503.
14. Henningsen, A.A., Pinborg, A., Lidegaard, O., Vestergaard, C.,

- Forman, J.L., Andersen, A.N. (2011) Perinatal outcome of singleton siblings born after assisted reproductive technology and spontaneous conception. *Fertility and Sterility*, 95(3): 959-963.
15. Wang, Y.A., Chughtai, A.A., Farquhar, C.M., Pollock, W., Lui, K., Sullivan, E.A. (2016) Increased incidence of gestational hypertension and preeclampsia after assisted reproductive technology treatment. *Fertility and Sterility*, 105(4): 920-926.
16. Luke, B., Brown, M.B., Wantman, E., Forestieri, N.E., Browne, M.L., Fisher, S.C., et al. (2017) Pregnancy, birth, and infant outcomes by maternal fertility status: the Massachusetts Outcomes Study of Assisted Reproductive Technology. *American Journal of Obstetrics and Gynecology*, 217(3): 327.e1-327.e14.
17. Palomba, S., de Wilde, M.A., Falbo, A., Koster, M.P., La Sala, G.B., Fauser, B.C. (2015) Pregnancy complications in women with polycystic ovary syndrome. *Human Reproduction Update*, 21(5): 575-592.
18. Bosdou, J.K., Anagnostis, P., Goulis, D.G., Lainas, G.T., Tarlatzis, B.C., Grimbizis, G.F., et al. (2020) Risk of gestational diabetes mellitus in women achieving singleton pregnancy spontaneously or after ART. *Human Reproduction Update*, 26(4): 514-544.
19. von Versen-Hoynck, F., Schaub, A.M., Chi, Y.Y., Chiu, K.H., Liu, J., Lingis, M., et al. (2019) Increased preeclampsia risk and reduced aortic compliance with in vitro fertilization cycles in the absence of a corpus luteum. *Hypertension*, 73(3): 640-649.
20. Saito, K., Kuwahara, A., Ishikawa, T., Morisaki, N., Miyado, M., Miyado, K., et al. (2019) Endometrial preparation methods for frozen-thawed embryo transfer associated with hypertensive disorders of pregnancy. *Human Reproduction*, 34(8): 1567-1575.
21. Ernstad, E.G., Wennerholm, U.B., Khatibi, A., Petzold, M., Bergh, C. (2019) Neonatal and maternal outcome after frozen embryo transfer: increased risks in programmed cycles. *American Journal of Obstetrics and Gynecology*, 221(2): 126.e1-126.e18.
22. Maheshwari, A., Pandey, S., Amalraj Raja, E., Shetty, A., Hamilton, M., Bhattacharya, S. (2018) Is frozen embryo transfer better for mothers and babies? *Human Reproduction Update*, 24(1): 35-58.
23. Masoudian, P., Nasr, A., de Nanassy, J., Fung-Kee-Fung, K., Bainbridge, S.A., El Demellawy, D. (2016) Oocyte donation pregnancies and risk of preeclampsia: systematic review and meta-analysis. *American Journal of Obstetrics and Gynecology*, 214(3): 328-339.
24. Storgaard, M., Loft, A., Bergh, C., Wennerholm, U.B., Sostrup, B., Bay, B., et al. (2017) Obstetric and neonatal complications in pregnancies conceived after oocyte donation: a systematic review and meta-analysis. *BJOG*, 124(4): 561-572.
25. Malchau, S.S., Loft, A., Larsen, E.C., Aaris Henningsen, A.K., Rasmussen, S., Andersen, A.N., et al. (2013) Perinatal outcomes in 375 children born after oocyte donation. *Fertility and Sterility*, 99(6): 1637-1643.
26. Sha, T., Yin, X., Cheng, W., Massey, I.Y. (2019) Pregnancy-related complications and perinatal outcomes resulting from transfer of cryopreserved versus fresh embryos in vitro fertilization: a meta-analysis. *Fertility and Sterility*, 109(2): 330-342.
27. Chen, Z.J., Shi, Y., Sun, Y., Zhang, B., Liang, X., Cao, Y., et al. (2016) Fresh versus frozen embryos for infertility in the polycystic ovary syndrome. *New England Journal of Medicine*, 375(6): 523-533.
28. Roberts, J.M., Escudero, C. (2012) The placenta in preeclampsia. *Pregnancy Hypertension*, 2(2): 72-83.
29. Kroener, L., Wang, E.T., Pisarska, M.D. (2016) Predisposing factors to abnormal first trimester placentation and the impact on fetal outcomes. *Seminars in Reproductive Medicine*, 34(1): 27-35.

30. Conrad, K.P. (2011) Maternal vasodilation in pregnancy: the emerging role of relaxin. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, 301(2): R267-R275.
31. Schwarze, J.E., Borda, P., Vasquez, P., Ortega, C., Villa, S., Crosby, J.A., et al. (2018) Is the risk of preeclampsia higher in donor oocyte pregnancies? A systematic review and meta-analysis. *JBRA Assisted Reproduction*, 22(1): 15-19.
32. Thomopoulos, C., Tsioufis, C., Michalopoulou, H., Makris, T., Papademetriou, V. (2013) Assisted reproductive technology and pregnancy-related hypertensive complications: a systematic review. *Journal of Human Hypertension*, 27(3): 148-157.
33. Wu, P., Haththotuwa, R., Kwok, C.S., Babu, A., Kotronias, R.A., Rushton, C., et al. (2017) Preeclampsia and future cardiovascular health: a systematic review and meta-analysis. *Circulation: Cardiovascular Quality and Outcomes*, 10(2): e003497.