

THE ASSOCIATION BETWEEN ESTRADIOL LEVELS ON DAY OF TRIGGER PREGNANCY OUTCOMES IN LETROZOLE STIMULATED FROZEN EMBRYO TRANSFER CYCLES

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INTRODUCTION

- Prior research evaluating letrozole for ovulation induction has shown that estradiol (E2) levels below the 25th percentile in intrauterine insemination cycles are associated with poorer outcomes (1)
- The degree of E2 suppression by letrozole varies among patients, and the impact of these reduced estradiol levels on endometrial preparation during frozen embryo transfer warrant further investigation

OBJECTIVE

To evaluate pregnancy outcomes relative to E2 level on the day of trigger in Letrozole stimulated frozen embryo transfer (LTZ-FET) cycles

METHODS

- Retrospective cohort study
- All autologous single blastocyst LTZ-FET cycles from January 2017 to November 2023
- Exclusion criteria: RPL, unmitigated uterine factor, use of GCs or donor gametes and cycles using gonadotropins and/or E2 supplementation to increase endometrial thickness
- Restricted cubic spline regression models were used to explore the potential nonlinear relationship between estradiol levels and live birth outcomes
- E2 was also categorized into two groups: <200pg/mL and ≥200pg/mL.
- Risk ratios (RR) and 95% confidence intervals were calculated to evaluate live birth among the defined estradiol level categories using Poisson regression models fitted with generalized estimating equations
- Outcomes were adjusted for age, BMI, and PGT-A use

RESULTS

Figure 1. Predicted probability of live birth as a function of estradiol (E2) levels at the time of trigger (N = 968 cycles)

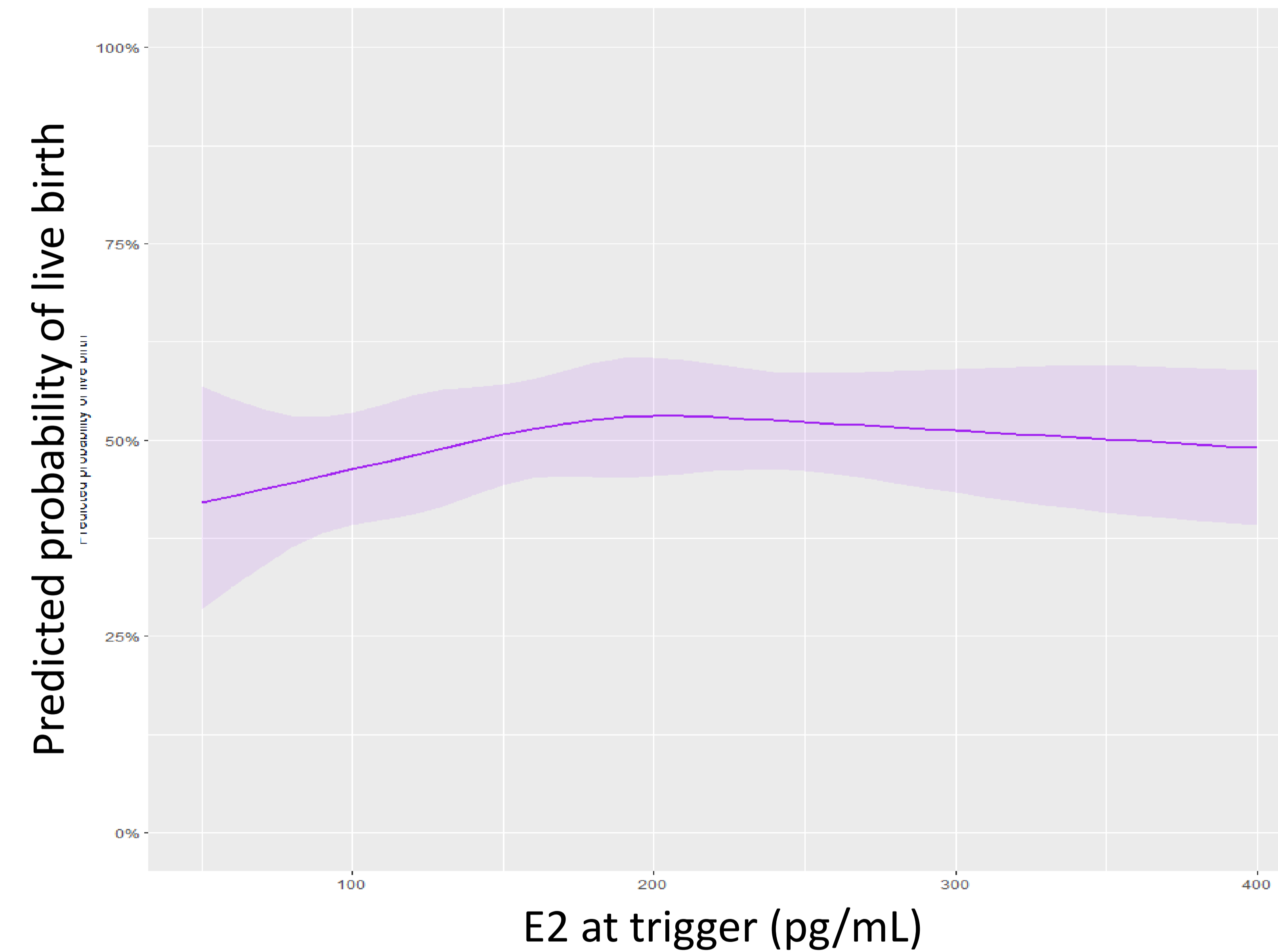


Table 1. Comparison of cycle characteristics between different E2 thresholds

	E2 ≥200.0 pg/mL	E2 <200.0 pg/mL
	Median (IQR)	Median (IQR)
Peak E2 level (pg/mL)	265.9 (226.9 – 344.0)	132.8 (104 - 163.1)
Progesterone level at trigger (ng/mL)	0.5 (0.4 - 0.7)	0.5 (0.3 - 0.7)
Progesterone level at first bhcg check (ng/mL)	26.3 (17.1 - 38.8)	25.6 (14.3 - 34.9)
LH level at trigger	9.1 (6.1 - 17.8)	6.7 (5.1 - 10.4)
Endometrial thickness (mm)	9.0 (8.1 - 10.3)	8.8 (8.1 – 10.0)
# of follicles >14mm	2.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)

Table 2. Comparison of clinical outcomes between different E2 thresholds

	E2 ≥200.0 pg/mL		E2 <200.0 pg/mL	
	N (%)	RR (95% CI)	N (%)	RR (95% CI)
Biochemical Pregnancy*	29 (10.2)	Ref	36 (9.3)	0.9 (0.5 - 1.3)
Clinical Pregnancy	250 (63.3)	Ref	345 (62.7)	1.0 (0.9 - 1.1)
Clinical Pregnancy Loss*	21 (7.7)	Ref	25 (6.8)	0.8 (0.5 - 1.4)
Live Birth	142 (45.8)	Ref	195 (45.5)	1.0 (0.9 - 1.2)

*losses calculated out of pregnancies
RR adjusted for age, BMI, PGT

CONCLUSIONS

- No significant association between E2 levels on day of trigger in LTZ-FET cycles and pregnancy outcomes was observed
- These findings suggest that while E2 plays a recognized role in endometrial receptivity, its direct influence on pregnancy outcomes in letrozole-stimulated FET cycles may not be as critical as previously thought

REFERENCES

1. Live birth associated with peak serum estradiol levels in letrozole intrauterine insemination cycles. New, Erika P. et al. Fertility and Sterility, Volume 119, Issue 5, 785 - 791