International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Pushparaj S et al. Int J Reprod Contracept Obstet Gynecol. 2026 Jun;15(6):1980-1984
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20261596

Original Research Article

Impact of Atosiban administration on live birth rates in patients undergoing frozen embryo transfer: a retrospective self-controlled study

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Received: 01 April 2026
Revised: 08 May 2026
Accepted: 11 May 2026

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ABSTRACT

Background: To evaluate the impact of Atosiban, an oxytocin receptor antagonist, on live birth rates (LBR) and other pregnancy outcomes in patients with a history of failed frozen embryo transfer (FET) cycles.
Methods: This was a retrospective, self-controlled study conducted at a single tertiary care center between January 2018 and December 2024. A cohort of 73 patients who had undergone at least one unsuccessful FET cycle (Cycle 1) without atosiban and a subsequent FET cycle with Atosiban administration (Cycle 2) were included. Each patient served as her own control. The primary outcome was the live birth rate. Secondary outcomes included biochemical pregnancy, clinical pregnancy, miscarriage, and implantation rates. Statistical analysis involved paired t-tests for continuous variables and Fisher's exact test for categorical outcomes.
Results: The administration of Atosiban in Cycle 2 was associated with a significant improvement in pregnancy outcomes. The live birth rate increased from 0% in Cycle 1 to 26.0% in Cycle 2 ($p<0.001$). Similarly, the clinical pregnancy rate rose from 2.7%-43.8% ($p<0.001$), and the biochemical pregnancy rate increased from 11.0%-65.8% ($p<0.001$). The implantation rate showed a non-significant increase from 50% in Cycle 1 to 55% in Cycle 2 ($p=0.372$).
Conclusions: In a self-controlled cohort of patients with previous FET failure, Atosiban administration at the time of embryo transfer was associated with a statistically and clinically significant increase in live birth rates. These findings support Atosiban as a valuable therapeutic option to improve implantation success in this challenging patient population.

Keywords: Atosiban, Frozen embryo transfer, Implantation failure, Live birth rate, Uterine contractility, IVF

INTRODUCTION

Successful embryo implantation is a complex and finely orchestrated process requiring a receptive endometrium, a viable embryo, and synchronized dialogue between them.[1] A critical factor influencing this process is uterine quiescence during the peri-implantation period. Excessive uterine contractility at the time of embryo transfer has been identified as a significant barrier to implantation, potentially causing the expulsion of the embryo from the uterine cavity or disrupting the delicate apposition and adhesion phases. Studies have demonstrated that high-frequency uterine contractions during embryo transfer are associated with significantly lower pregnancy rates in in vitro fertilization (IVF) cycles.[2,3] Atosiban, a synthetic peptide, acts as a competitive antagonist of oxytocin and vasopressin V1A receptors. By inhibiting oxytocin-induced myometrial contractions, it promotes uterine quiescence. While its primary licensed use is for the management of preterm labor, its potential to improve implantation outcomes in assisted reproductive technology (ART) has been a subject of considerable research and

debate.[4] Recent insights suggest that Atosiban may also enhance endometrial receptivity by suppressing inflammation-related pathways and reducing intracellular calcium levels in the endometrium. The existing literature presents a conflicting picture regarding the efficacy of Atosiban in improving IVF outcomes.[5-10] Some systematic reviews and meta-analyses suggest that Atosiban can improve clinical pregnancy rates, particularly in select populations such as those with repeated implantation failure (RIF).[11-14] However, other large randomized controlled trials (RCTs) and retrospective studies have failed to demonstrate a significant benefit in unselected or general IVF/FET populations, particularly concerning the primary outcome of live birth rate.[15,16]

This discrepancy suggests that the benefit of Atosiban may be confined to specific patient subgroups where abnormal uterine contractility is a more prominent etiological factor. Patients who have experienced previous FET failures represent one such subgroup. Our personal understanding, grounded in clinical observation, suggests that inter-patient variability in uterine response to the transfer procedure itself may be a hidden confounder in many large-scale trials. By utilizing a self-controlled design, we aim to isolate the effect of Atosiban by minimizing the confounding effects of inter-patient variability in embryo quality, endometrial response, and underlying pathology. This study investigates the efficacy of Atosiban in a cohort of patients who had previously failed a FET cycle without its use.

METHODS

Study design and setting

This was a retrospective, single-center, self-controlled study conducted at the Institute of Reproductive Medicine, Madras Medical Mission, Chennai, India. The study included data from patients undergoing FET cycles between January 2018 and December 2024.

Participants

We identified patients from our electronic medical records who had undergone at least two FET cycles, where the first cycle was unsuccessful (Cycle 1, no Atosiban) and the subsequent cycle included the administration of Atosiban (Cycle 2). The decision to use Atosiban in Cycle 2 was made on a clinical basis by the treating physician, typically in patients with previous implantation failure The study participants were selected based on specific inclusion and exclusion criteria. Patients were included if they were aged between 21 and 45 years, had a baseline Follicle-Stimulating Hormone (FSH) level of less than 10 IU/l, and maintained an endometrial thickness of at least 8 mm in both cycles. Additionally, the availability of at least one good quality embryo after thawing was required for inclusion. Conversely, patients were excluded from the study if they had known congenital uterine anomalies, adenomyosis,fibroid uterus an endometrial thickness of less than 8 mm on the day of progesterone initiation, or if their FET cycles were cancelled due to poor quality embryos post-thaw. Individuals with a known allergy to Atosiban were also excluded. A total of 73 patients met these criteria and were included in the final analysis. During the study period, 1,107 FET cycles were performed at our center, of which 825 were first FET cycles and 282 were repeat FET cycles.

Intervention: Atosiban protocol

In Cycle 2, patients received intravenous Atosiban (37.5 mg in 5 ml) according to established protocols. A slow intravenous bolus of 6.75 mg (0.9 ml) was administered 30 minutes prior to embryo transfer. Following the transfer, an infusion was continued at 18 mg/h for the first hour, followed by 6 mg/h for the subsequent two hours. The total dose is administered over approximately 3.5 hours.

Frozen embryo transfer protocol

Endometrial preparation was performed using hormonal replacement therapy (HRT), ovulation induction with letrozole, or modified natural cycle monitoring. Progesterone supplementation (100 mg daily intramuscularly) was initiated once the endometrial thickness reached ≥ 8 mm and serum progesterone was < 1.5 ng/ml. Embryo transfer was performed under transabdominal ultrasound guidance using a soft catheter 4,5 or 6 days after progesterone initiation for cleavage stage (day 3), morula (day 4), and blastocyst (day 5) transfers, respectively.

Outcome measures

The primary outcome was the live birth rate (LBR), defined as the delivery of a live-born infant after 24 weeks of gestation. Secondary outcomes included biochemical pregnancy rate (positive serum β-HCG >10 mIU/ml), clinical pregnancy rate (gestational sac with fetal heartbeat at 6-7 weeks), implantation rate, miscarriage rate, and neonatal outcomes.

Statistical analysis

Continuous variables were presented as mean±standard deviation (SD) and compared using paired t-tests. Categorical variables were presented as frequencies and percentages. Given the zero live birth rate in the control group (Cycle 1), Fisher's exact test was used for primary and secondary outcomes. A p-value<0.05 was considered statistically significant.

RESULTS

Baseline and treatment characteristics

The study included 73 patients with a mean age of 32.52±4.46 years and a mean BMI of 27.22±3.84 kg/m². The mean duration of infertility was 5.68±3.07 years.

Primary subfertility accounted for 53% of cases, while secondary subfertility was 47%. Causes of subfertility were diverse, with male factor being the most common (42%), followed by unexplained infertility (25%), female factor (18%), and both factors (15%) (Figures 1 and 2).

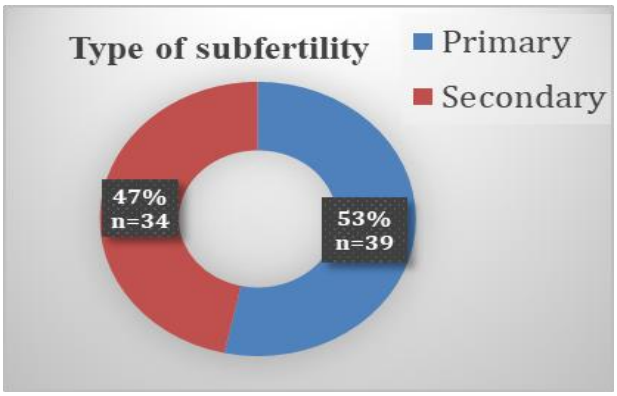

Figure 1: Type of subfertility.

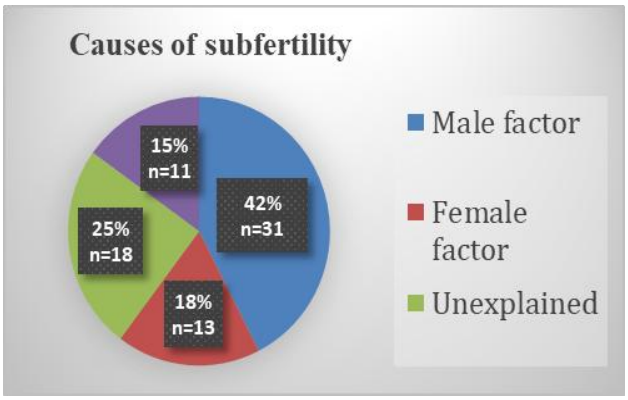

Figure 2: Causes of subfertility.

Table 1: Baseline patient characteristics.

Parameter	Mean	SD
Age (years)	32.52	4.46
BMI (kg/m²)	27.22	3.84
Infertility duration (years)	5.68	3.07

Treatment characteristics

Table 2 summarizes the treatment characteristics for Cycle 1 (no Atosiban) and Cycle 2 (with Atosiban). Endometrial thickness (ET) was comparable between the two cycles (8.72±1.15 mm in Cycle 1 vs. 8.92±1.18 mm in Cycle 2, p=0.1985), indicating no significant difference in endometrial preparation. The mean number of embryos transferred was also similar (2.33±0.80 in Cycle 1 vs. 2.12±0.67 in Cycle 2). There was a shift in embryo transfer distribution in Cycle 2, with a higher proportion of 2-embryo transfers (67% vs. 36% in Cycle 1) and a lower proportion of 3-embryo transfers (26% vs. 56% in Cycle 1). The day of embryo transfer also showed a trend towards later transfers in Cycle 2, with Day 5 transfers increasing from 18%-29%.

Table 2: Mean ET and mean embryos.

Parameter	Cycle 1	Cycle 2	P value
Mean ET (mm)	8.72±1.15	8.92±1.18	0.1985
Mean embryos	2.33±0.80	2.12±0.67	NA

Table 3: Comparison of pregnancy outcomes between cycle 1 (control) and cycle 2 (Atosiban).

Outcome	Cycle 1 (n=73)	Cycle 2 (n=73)	P value
Biochemical pregnancy	11.0% (8/73)	65.8% (48/73)	<0.001
Clinical pregnancy	2.7% (2/73)	43.8% (32/73)	<0.001
Miscarriage rate	2.7% (2/73)	21.9% (16/73)	<0.001
Live birth rate	0% (0/73)	26.0% (19/73)	<0.001
Implantation rate	50%	55%	0.372

Table 4: Gestational age at delivery (cycle 2).

Gestational age (weeks)	N (%)
≥37	9(52)
34-36+6	4(19)
28-33+6	4(19)
<28	2(10)

Pregnancy and neonatal outcomes

The administration of Atosiban was associated with a dramatic improvement in pregnancy outcomes (Table 3). The live birth rate increased from 0% in Cycle 1 to 26.0% in Cycle 2 (p<0.001). Clinical pregnancy rates rose from 2.7% to 43.8% (p<0.001).

In the cycle 1, of the 11% biochemical pregnancies, 2.7% converted to clinical pregnancies all of which resulted in miscarriage. In the cycle 2, of the 65.8% biochemical pregnancies, 69.6% converted to clinical pregnancies, and 59.4% of clinical pregnancies resulted in live births.

Neonatal outcomes for the 19 live births in Cycle 2 showed a mean gestational age of 36.5±2.5 weeks and a mean birth weight of 2.67±0.5 kg. Of these, 52% were delivered at ≥37 weeks. Table 4 illustrates the Gestational age at delivery in Cycle 2

DISCUSSION

The present study demonstrates that Atosiban administration significantly improves live birth rates in

patients with a history of failed FET cycles. The increase from 0% to 26.0% LBR is both statistically and clinically profound in a self-controlled cohort. The results of our study are consistent with the study done by Wang R et al, 2023 which showed that Atosiban was associated with higher clinical pregnancy rate (RR=1.54, 95% CI: 1.365-1.735, p< 0.001) in patients with recurrent implantation failure.[11]

A retrospective study Chou PY et al, 2011 aimed to investigate the use of an oxytocin antagonist in improving the pregnancy outcome of in vitro fertilization-embryo transfer (IVF-ET) in patients with repeated implantation failure (RIF) and concluded that significantly higher implantation rate of 30.21% (p=0.0006), clinical pregnancy rate of 37.5% (p=0.0057) and live birth rate of 35%(p=0.0031) was noted in Atosiban group compared with control group which was similar to the results of our study.[12]

A prospective cohort study done by Lan VT et al, 2012 examined the effects of Atosiban on uterine contraction, implantation rate (IR) and clinical pregnancy rate (CPR) in women undergoing IVF/embryo transfer.[13] The IR per transfer and CPR per cycle were 13.9% and 43.7%, respectively which echoed the results of our study.

In a pooled meta-analysis done by Schwarze JE et al, in 1025 patients, Atosiban increased clinical pregnancy rates (pooled OR 1.47, 95% CI 1.18-1.82) similar to the results of our study.[14]

Though the existing literature presents a conflicting picture regarding the efficacy of Atosiban in improving IVF outcomes, in the present study Atosiban has proved its effectiveness in improving the clinical pregnancy and live birth rate in a cohort of patients who had previously failed a FET cycle without its use.[5]

Strengths and limitations

Strengths of this study include the self-controlled design, which effectively minimizes confounding variables related to individual patient characteristics. By using each patient as her own control, we achieved a more direct assessment of the intervention's effect. Additionally, our focus on a specific and challenging patient population—those with a history of failed FET cycles—allows for a more precise evaluation of Atosiban's efficacy in a group that may benefit most from such interventions.

However, this study has several limitations. First, the retrospective nature means that treatment decisions were not randomized. Second, we did not quantify uterine waves before and after Atosiban administration. Third, we lacked information on embryo ploidy status for most patients, as preimplantation genetic testing was not routinely performed. Fourth, we did not assess long-term neonatal outcomes beyond birth weight and gestational age. Finally, the study was conducted at a single center, which may limit generalizability to other settings. Future research should include larger, prospective randomized controlled trials incorporating direct measurements of uterine contractility, assessment of embryo ploidy, and long-term follow-up of neonatal outcomes. Further investigation into specific patient subgroups that may benefit most from Atosiban would also be valuable.

CONCLUSION

In a self-controlled cohort of patients with previous FET failure, Atosiban administration at the time of embryo transfer was associated with a statistically and clinically significant increase in live birth rates, biochemical pregnancy rates, and clinical pregnancy rates. These findings support Atosiban as a valuable therapeutic option to improve implantation success in this challenging patient population. The dramatic improvement from a patient's own prior failed cycle underscores the clinical utility of Atosiban in this specific setting. Further large-scale randomized controlled trials are warranted to confirm these results and explore optimal patient selection criteria.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T, et al. Recurrent implantation failure: definition and management. Reprod Biomed Online. 2014;28(1):14-38.
2. Zhu L, Che HS, Xiao L, Li YP. Uterine peristalsis before embryo transfer affects the chance of clinical pregnancy in fresh and frozen-thawed embryo transfer cycles. Hum Reprod. 2014;29(6):1238-43.
3. Buddhabunyakan N, Sothornwit J, Seejorn K, Buppasiri P, Salang L. Effects of atosiban on uterine peristalsis following frozen embryo transfer: a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2021;265:96-101.
4. Pierzynski P, Reinheimer TM, Kuczynski W. Oxytocin antagonists may improve infertility treatment. Fertil Steril. 2007;88(1):213.e19-22.
5. Cai H, Liu S, Chen L, Xie J, Yang C, Li W, et al. Effectiveness of atosiban in women with previous single implantation failure undergoing frozen-thawed blastocyst transfer: study protocol for a randomised controlled trial. BMJ Open. 2023;13(10):e076390.
6. Mishra V, Agarwal H, Goel S, Roy P, Choudhary S, Lamba S. A prospective case-control trial to evaluate and compare the efficacy and safety of atosiban versus placebo in in vitro fertilization–embryo transfer program. J Hum Reprod Sci. 2018;11(2):155-60.
7. Moraloglu O, Tonguc E, Var T, Zeyrek T, Batioglu S. Treatment with oxytocin antagonists before

embryo transfer may increase implantation rates after IVF. Reprod Biomed Online. 2010;21(3):338-43.
8. Ng EHY, Li RHW, Chen L, Lan VT, Tuong HM, Quan S. A randomized double-blind comparison of atosiban in patients undergoing IVF treatment. Hum Reprod. 2014;29(12):2687-94.
9. Wu MH, Lin CW, Su PF, Lai EC, Sie FC, Mau YL, et al. Atosiban and pregnancy outcomes following in vitro fertilization treatment for infertile women requiring one, two, or more embryo transfer cycles: a longitudinal cohort study. Reprod Sci. 2020;27(3):853-9.
10. Yuan C, Song H, Fan L, Su S, Dong B. The effect of atosiban on patients with difficult embryo transfers undergoing in vitro fertilization–embryo transfer. Reprod Sci. 2019;26(12):1613-7.
11. Wang R, Huang H, Tan Y, Xia G. Efficacy of atosiban for repeated embryo implantation failure: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2023;14:1161707.
12. Chou PY, Wu MH, Pan HA, Hung KH, Chang FM. Use of an oxytocin antagonist in in vitro fertilization–embryo transfer for women with repeated implantation failure: a retrospective study. Taiwan J Obstet Gynecol. 2011;50(2):136-40.
13. Lan VT, Khang VN, Nhu GH, Tuong HM. Atosiban improves implantation and pregnancy rates in patients with repeated implantation failure. Reprod Biomed Online. 2012;25(3):254-60.
14. Schwarze JE, Crosby J, Mackenna A. Atosiban improves the outcome of embryo transfer: a systematic review and meta-analysis of randomized and non-randomized trials. JBRA Assist Reprod. 2020;24(4):421-7.
15. Yang Y, Luo R, Qin S, Zhu W, Yang M, Zhu D, et al. The effect of atosiban on pregnancy outcomes in different FET cycles: a single-center matched retrospective cohort study. Front Endocrinol (Lausanne). 2025;16:1547694.
16. Huang QY, Rong MH, Lan AH, Lin XM, Lin XG, He RQ, et al. The impact of atosiban on pregnancy outcomes in women undergoing in vitro fertilization–embryo transfer: a meta-analysis. PLoS One. 2017;12(4):e0175501.

Cite this article as: Pushparaj S, Kundavi KM, Rashmi GV, Geetha V, Ranji GC, Asokan Y, et al. Impact of atosiban administration on live birth rates in patients undergoing frozen embryo transfer: a retrospective self-controlled study. Int J Reprod Contracept Obstet Gynecol 2026;15:1980-4.