

Bölüm 5

Tedavi Gebeliklerinin Perinatal Sonuçları



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Giriş

Günümüzde infertilite nedeniyle olan başvuru oranlarındaki artış, tedavi gebelikleri ve sonuçları üzerine yapılan çalışmaların ivme kazanmasını sağlamıştır. Tedavi gebeliklerinin spontan gebeliklere göre daha olumsuz obstetrik ve perinatal sonuçlara yol açtığı bilinmektedir. Ancak bu durumun primer olarak subfertilite ya da üremeye yardımcı tedavi (ÜYTE/ART) teknikleri ile ilişkili olduğu konusu tartışmalıdır. Son olarak güncel bir derlemede bu olumsuz sonuçlardan her iki faktörün de sorumlu olduğu belirtilmiştir [1].

Subfertilite sonrası gelişen gerek spontan gebelikler gerekse intrauterin inseminasyon (IUI) ve ÜYTE (ART) gebelikleri; fertilite sorunu yaşanmayan spontan gebeliklere göre farklı perinatal sonuçlarla ilişkilidir (Tablo 1). Dolayısıyla; tedavi gebeliklerinde daha yakın antenatal takip ihtiyacı olduğu, hatta bazı tarama testlerinin yorumunda ÜYTE (ART) gebeliklerinin daha farklı değerlendirilmesi gerektiği unutulmamalıdır. Zira; ÜYTE (ART) gebeliklerindeki plasentasyon farklılığına bağlı olarak biyokimyasal belirteçlerde gözlenebilen değişiklikler, tarama testlerinde yalancı pozitifliğe yol açabilir [2]. Bu bölümde, tedavi gebelikleri IUI gebelikleri ve ÜYTE (ART) gebelikleri olmak üzere 2 ana başlık altında ele alınacaktır.

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sız olarak da antepartum kanama, artmış sezaryan oranı, gestasyonel hipertansiyon, erken membran rüptürü, düşük doğum ağırlığı, preterm doğum ve perinatal mortalite açısından risk altında olduğundan 'yüksek riskli gebelik' olarak kabul edilmeli ve yakın antenatal takibe alınmalıdır. Ayrıca, COVID-19 aşılarının erkek ya da kadın infertilitesine yol açmadığı ancak COVID-19 hastalığı geçiren erkeklerde sperm miktarının önemli oranda azaldığı bilgisi ışığında, infertilite tedavisi planlanan çiftlerin mümkünse tedavi öncesi COVID-19 aşılarını tamamlamaları, aşısız olan gebelerin ise ilk trimester sonrası aşı olmaları tavsiye edilmelidir.

Kaynaklar

1. Berntsen S, Soderstrom-Anttila V, Wennerholm UB, Laivuori H, Loft A, Oldereid NB, et al. The health of children conceived by ART: 'the chicken or the egg?'. *Hum Reprod Update* 2019;25(2):137-58.
2. Gjerris AC, Tabor A, Loft A, Christiansen M, Pinborg A. First trimester prenatal screening among women pregnant after IVF/ICSI. *Hum Reprod Update* 2012;18(4):350-9.
3. Malchau SS, Loft A, Henningsen AK, Nyboe Andersen A, Pinborg A. Perinatal outcomes in 6,338 singletons born after intrauterine insemination in Denmark, 2007 to 2012: the influence of ovarian stimulation. *Fertil Steril* 2014;102(4):1110-6 e2.
4. Zegers-Hochschild F, Nygren KG, Adamson GD, de Mouzon J, Lancaster P, Mansour R, et al. The International Committee Monitoring Assisted Reproductive Technologies (ICMART) glossary on ART terminology. *Fertil Steril* 2006;86(1):16-9.
5. Group ECW. Intrauterine insemination. *Hum Reprod Update* 2009;15(3):265-77.
6. van Rumste MM, den Hartog JE, Dumoulin JC, Evers JL, Land JA. Is controlled ovarian stimulation in intrauterine insemination an acceptable therapy in couples with unexplained non-conception in the perspective of multiple pregnancies? *Hum Reprod* 2006;21(3):701-4.
7. Luke B, Gopal D, Cabral H, Stern JE, Diop H. Adverse pregnancy, birth, and infant outcomes in twins: effects of maternal fertility status and infant gender combinations; the Massachusetts Outcomes Study of Assisted Reproductive Technology. *Am J Obstet Gynecol* 2017;217(3):330 e1- e15.
8. Yilmaz NK, Sargin A, Erkilinc S, Ozer I, Engin-Ustun Y. Does ovulation induction and intrauterine insemination affect perinatal outcomes in singletons? *J Matern Fetal Neonatal Med* 2018;31(1):14-7.
9. Ombelet W, Martens G, De Sutter P, Gerris J, Bosmans E, Ruysinck G, et al. Perinatal outcome of 12,021 singleton and 3108 twin births after non-IVF-assisted reproduction: a cohort study. *Hum Reprod* 2006;21(4):1025-32.
10. Klemetti R, Gissler M, Hemminki E. Comparison of perinatal health of children born from IVF in Finland in the early and late 1990s. *Hum Reprod* 2002;17(8):2192-8.
11. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. *Hum Reprod Update* 2012;18(5):485-503.
12. Qin JB, Sheng XQ, Wu D, Gao SY, You YP, Yang TB, et al. Worldwide prevalence of adverse pregnancy outcomes among singleton pregnancies after in vitro fertilization/intracytoplasmic sperm injection: a systematic review and meta-analysis. *Arch Gynecol Obstet* 2017;295(2):285-301.



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13. Opdahl S, Henningsen AA, Tiitinen A, Bergh C, Pinborg A, Romundstad PR, et al. Risk of hypertensive disorders in pregnancies following assisted reproductive technology: a cohort study from the CoNARTaS group. *Hum Reprod* 2015;30(7):1724-31.
14. Fertilisation H, Authority E. Improving outcomes for fertility patients: Multiple births. A statistical report 2011.
15. Busnelli A, Dallagiovanna C, Reschini M, Paffoni A, Fedele L, Somigliana E. Risk factors for monozygotic twinning after in vitro fertilization: a systematic review and meta-analysis. *Fertil Steril* 2019;111(2):302-17.
16. Gazete R. Üremeye yardımcı tedavi uygulamaları ve üremeye yardımcı tedavi merkezleri hakkında yönetmelik. *Resmi Gazete* 2010;6:20100306-10.
17. Yilmaz N, Engin-Ustun Y, Inal H, Gorkem U, Bardakci Y, Gulerman C. The impact of single embryo transfer policy on pregnancy outcomes after legislative change. *Gynecol Endocrinol* 2013;29(6):600-2.
18. Skiadas CC, Missmer SA, Benson CB, Acker D, Racowsky C. Spontaneous reduction before 12 weeks' gestation and selective reduction similarly extend time to delivery in in vitro fertilization of trichorionic-triamniotic triplets. *Fertil Steril* 2011;95(2):596-9.
19. Pezeshki K, Feldman J, Stein DE, Lobel SM, Grazi RV. Bleeding and spontaneous abortion after therapy for infertility. *Fertil Steril* 2000;74(3):504-8.
20. Ludwig M, Kaisi M, Bauer O, Diedrich K. Heterotopic pregnancy in a spontaneous cycle: do not forget about it! *Eur J Obstet Gynecol Reprod Biol* 1999;87(1):91-3.
21. Noci I, Saltarelli O, Coccia E, Messo A, Livi C, Massi GB, et al. Interference of exogenous HCG on pregnancy tests. *Acta Eur Fertil* 1987;18(6):391-3.
22. Zhang B, Cui L, Tang R, Ding L, Yan L, Chen ZJ. Reduced Ectopic Pregnancy Rate on Day 5 Embryo Transfer Compared with Day 3: A Meta-Analysis. *PLoS One* 2017;12(1):e0169837.
23. Londra L, Moreau C, Strobino D, Garcia J, Zacur H, Zhao Y. Ectopic pregnancy after in vitro fertilization: differences between fresh and frozen-thawed cycles. *Fertil Steril* 2015;104(1):110-8.
24. Yilmaz N, Kara M, Coskun B, Kaba M, Erkilinc S, Yenicesu O, et al. Perinatal outcomes and cost-effectivity of the assisted reproduction pregnancies with advanced age: A retrospective analysis. *J Obstet Gynaecol* 2017;37(4):450-3.
25. Hung TH, Hsieh CC, Hsu JJ, Chiu TH, Lo LM, Hsieh TT. Risk factors for placenta previa in an Asian population. *Int J Gynaecol Obstet* 2007;97(1):26-30.
26. Pinborg A, Wennerholm UB, Romundstad LB, Loft A, Aittomaki K, Soderstrom-Anttila V, et al. Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis. *Hum Reprod Update* 2013;19(2):87-104.
27. Aflatoonian A, Mansoori Moghaddam F, Mashayekhy M, Mohamadian F. Comparison of early pregnancy and neonatal outcomes after frozen and fresh embryo transfer in ART cycles. *J Assist Reprod Genet* 2010;27(12):695-700.
28. Belva F, Henriët S, Van den Abbeel E, Camus M, Devroey P, Van der Elst J, et al. Neonatal outcome of 937 children born after transfer of cryopreserved embryos obtained by ICSI and IVF and comparison with outcome data of fresh ICSI and IVF cycles. *Hum Reprod* 2008;23(10):2227-38.
29. Wong KM, van Wely M, Mol F, Repping S, Mastenbroek S. Fresh versus frozen embryo transfers in assisted reproduction. *Cochrane Database Syst Rev* 2017;3:CD011184.
30. Maheshwari A, Pandey S, Shetty A, Hamilton M, Bhattacharya S. Obstetric and perinatal outcomes in singleton pregnancies resulting from the transfer of frozen thawed versus fresh embryos generated through in vitro fertilization treatment: a systematic review and meta-analysis. *Fertil Steril* 2012;98(2):368-77 e1-9.



31. Zhao J, Xu B, Zhang Q, Li YP. Which one has a better obstetric and perinatal outcome in singleton pregnancy, IVF/ICSI or FET?: a systematic review and meta-analysis. *Reprod Biol Endocrinol* 2016;14(1):51.
32. Sha T, Yin X, Cheng W, Massey IY. Pregnancy-related complications and perinatal outcomes resulting from transfer of cryopreserved versus fresh embryos in vitro fertilization: a meta-analysis. *Fertil Steril* 2018;109(2):330-42 e9.
33. Evans J, Hannan NJ, Edgell TA, Vollenhoven BJ, Lutjen PJ, Osianlis T, et al. Fresh versus frozen embryo transfer: backing clinical decisions with scientific and clinical evidence. *Hum Reprod Update* 2014;20(6):808-21.
34. Shih W, Rushford DD, Bourne H, Garrett C, McBain JC, Healy DL, et al. Factors affecting low birthweight after assisted reproduction technology: difference between transfer of fresh and cryopreserved embryos suggests an adverse effect of oocyte collection. *Hum Reprod* 2008;23(7):1644-53.
35. Shaw L, Sneddon SF, Brison DR, Kimber SJ. Comparison of gene expression in fresh and frozen-thawed human preimplantation embryos. *Reproduction* 2012;144(5):569-82.
36. Singh B, Reschke L, Segars J, Baker VL. Frozen-thawed embryo transfer: the potential importance of the corpus luteum in preventing obstetrical complications. *Fertil Steril*. 2020 Feb;113(2):252-7.
37. Glujovsky D, Blake D, Farquhar C, Bardach A. Cleavage stage versus blastocyst stage embryo transfer in assisted reproductive technology. *Cochrane Database Syst Rev* 2012(7):CD002118.
38. Maheshwari A, Kalampokas T, Davidson J, Bhattacharya S. Obstetric and perinatal outcomes in singleton pregnancies resulting from the transfer of blastocyst-stage versus cleavage-stage embryos generated through in vitro fertilization treatment: a systematic review and meta-analysis. *Fertil Steril* 2013;100(6):1615-21 e1-10.
39. Wang X, Du M, Guan Y, Wang B, Zhang J, Liu Z. Comparative neonatal outcomes in singleton births from blastocyst transfers or cleavage-stage embryo transfers: a systematic review and meta-analysis. *Reprod Biol Endocrinol* 2017;15(1):36.
40. Lambalk CB, Banga FR, Huirne JA, Toftager M, Pinborg A, Homburg R, et al. GnRH antagonist versus long agonist protocols in IVF: a systematic review and meta-analysis accounting for patient type. *Hum Reprod Update* 2017;23(5):560-79.
41. Toftager M, Bogstad J, Lossl K, Praetorius L, Zedeler A, Bryndorf T, et al. Cumulative live birth rates after one ART cycle including all subsequent frozen-thaw cycles in 1050 women: secondary outcome of an RCT comparing GnRH-antagonist and GnRH-agonist protocols. *Hum Reprod* 2017;32(3):556-67.
42. Tomas C, Toftager M, Lossl K, Bogstad J, Praetorius L, Zedeler A, et al. Perinatal outcomes in 521 gestations after fresh and frozen cycles: a secondary outcome of a randomized controlled trial comparing GnRH antagonist versus GnRH agonist protocols. *Reprod Biomed Online* 2019;39(4):659-64.
43. Heijnen EM, Eijkemans MJ, Hughes EG, Laven JS, Macklon NS, Fauser BC. A meta-analysis of outcomes of conventional IVF in women with polycystic ovary syndrome. *Hum Reprod Update* 2006;12(1):13-21.
44. Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. *Hum Reprod Update* 2006;12(6):673-83.
45. Reefhuis J, Honein MA, Schieve LA, Correa A, Hobbs CA, Rasmussen SA, et al. Assisted reproductive technology and major structural birth defects in the United States. *Hum Reprod* 2009;24(2):360-6.
46. Davies MJ, Moore VM, Willson KJ, Van Essen P, Priest K, Scott H, et al. Reproductive technologies and the risk of birth defects. *N Engl J Med* 2012;366(19):1803-13.



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47. Bonduelle M, Van Assche E, Joris H, Keymolen K, Devroey P, Van Steirteghem A, et al. Prenatal testing in ICSI pregnancies: incidence of chromosomal anomalies in 1586 karyotypes and relation to sperm parameters. *Hum Reprod* 2002;17(10):2600-14.
48. Hvidtjorn D, Grove J, Schendel D, Svaerke C, Schieve LA, Uldall P, et al. Multiplicity and early gestational age contribute to an increased risk of cerebral palsy from assisted conception: a population-based cohort study. *Hum Reprod* 2010;25(8):2115-23.
49. Sandin S, Nygren KG, Iliadou A, Hultman CM, Reichenberg A. Autism and mental retardation among offspring born after in vitro fertilization. *JAMA* 2013;310(1):75-84.
50. Hart R, Norman RJ. The longer-term health outcomes for children born as a result of IVF treatment: Part I--General health outcomes. *Hum Reprod Update* 2013;19(3):232-43.
51. Belva F, Bonduelle M, Roelants M, Michielsen D, Van Steirteghem A, Verheyen G, et al. Semen quality of young adult ICSI offspring: the first results. *Hum Reprod* 2016;31(12):2811-20.
52. Belva F, Roelants M, Vloeberghs V, Schiettecatte J, Evenepoel J, Bonduelle M, et al. Serum reproductive hormone levels and ultrasound findings in female offspring after intracytoplasmic sperm injection: first results. *Fertil Steril* 2017;107(4):934-9.
53. Williams CL, Bunch KJ, Stiller CA, Murphy MF, Botting BJ, Wallace WH, et al. Cancer risk among children born after assisted conception. *N Engl J Med* 2013;369(19):1819-27.
54. ESHRE COVID-19 Working Group, Ata B, Gianaroli L, Lundin K, Mcheik S, Mocanu E, Rautakallio-Hokkanen S, Tapanainen JS, Vermeulen N, Veiga A. Outcomes of SARS-CoV-2 infected pregnancies after medically assisted reproduction. *Hum Reprod*. 2021 Oct 18;36(11):2883-90.