Austin Journal of Invitro Fertilization

Open Access

Austin Publishing Group

Mini Review

The Effect Postnatal and Long-Term Outcome of Assisted Reproductive Technique on Newborns

Türker G*
Department of Pediatrics, Kocaeli University, Turkey

***Corresponding author:** GülcanTürker, Kocaeli University, Faculty of Medicine, Department of Pediatrics, Division of Neonatology, Turkey

Received: October 07, 2014; **Accepted:** November 13, 2014; **Published:** December 31, 2014

Abstract

Assisted Reproductive Technique rates (ART) are increasing worldwide and ART related births are1.4 % of U.S. births. Parallel to the rise in ART rates, publications that demonstrate intrauterine growth retardation, premature birth, perinatal mortality, very low birth weight, large birth weight and congenital anomalies as contributing factors for poor perinatal outcomes have also increased. Preterm delivery increase morbidity due to the conditions associated with prematurity including intraventricular hemorrhage, periventricular leukomalacia, necrotizing enterocolitis, retinopathy of prematurity, and respiratory distress syndrome thus cerebral palsy associated with PVL and mortality increased. The association of IVF with longer term clinical events has not been fully resolved but also the in-vitro techniques, the causes of infertility, the controlled ovarian stimulation, culture media, and possibly additional freezing or vitrification procedures seem to play a role. These increased risks are Multifactorial and related both ART procedures and underlying infertility. Therefore there have to be investigate risks of individual birth defects and disentangle the inter-related effects of different types of infertility and the multiple aspects of ART and the effect of ART procedures and underlying infertility on perinatal mortality and morbidity and on long-term outcome of babies.

Keywords: Assisted reproductive technique; *In vitro* fertilization; Morbidity; Mortality; Term newborn; Preterm newborn

Introduction

Assisted Reproductive Technique rates (ART) are increasing worldwide and ART related births are1.4 % of U.S. births [1]. Parallel to the rise in ART rates, publications that demonstrate Intrauterine Growth Retardation (IUGR), premature birth, perinatal mortality, Very Low Birth Weight (VLBW), large birth weight and congenital anomalies as contributing factors for poor perinatal outcomes have also increased [1-8].

Multiple pregnancies

Multiple pregnancies are associated with significantly higher risk than singleton pregnancies for both the mother and the babies. Maternal ante partum, intrapartum and postpartum complications are more frequent, as are perinatal squeal. Although multiple pregnancy is associated with significantly increased maternal and perinatal morbidity and mortality, (especially related preterm birth) as well as increased costs to the National Health Service, multiple birth rate in ART pregnancies is still high with this rate of 24%.The neonatal mortality rate of twins is six to seven times that of singleton pregnancies, at 18 per 1000 live births, whereas the neonatal mortality of triplets and higher order multiples reaches 39.6 per 100 live births [9]. The main reason for the elevated perinatal mortality rate seen in multiple pregnancies is the effects of preterm birth. Therefore NICE guidelines for embryo transfer strategies in *In-Vitro* Fertilization (IVF) are developed [10,11] and the elective single embryo transfer significantly reduces the risk of multiple pregnancy by up to 17-foldwhen compared to double embryo transfer [12]. Helmerhorst FM et al's have reported in their review that singleton pregnancies from ART have a significantly worse perinatal outcome than non-assisted singleton pregnancies, but this is less so for twin pregnancies. In twin pregnancies, perinatal mortality is about 40% lower after assisted compared with natural conception [3]. Also Frangez HB et al' shave reported up to 1,5 times higher incidence of preterm birth in women conceiving singletons in an IVF procedure compared to naturally conceiving controls in their latest study. They researched the factors from the IVF procedure as well as women's own risk factors for preterm birth contributed to an increased rate of preterm birth after an IVF procedure. In the IVF population, they found that body mass index plays a far more important role in preterm birth than in the fertile population. In their research, preterm birth reoccurrence in IVF group was less than expected, which they explained by the surgical correction of gynecological pathology and, where necessary, it's being combined with cerclage. They could not found any risk factors for preterm birth related to the IVF procedure [13]. Therefore we may suggest that prematurity is still a major problem in singletons from ART group.

Prematurity

Pandey et al showed poorer obstetric and perinatal outcomes in singleton pregnancies resulting from IVF or Intracytoplazmicsperm Injection (ICSI) compared with naturally conceived singletons in their recent meta-analysis [6]. Preterm delivery increase morbidity due to the conditions associated with prematurity including intraventricular hemorrhage, Periventricular Leukomalacia (PVL), necrotizing enterocolitis, retinopathy of prematurity, and respiratory distress syndrome thus cerebral palsy associated with PVL and mortality increased [11]. Also the other meta-analyses of infants born

Citation: Türker G. The Effect Postnatal and Long-Term Outcome of Assisted Reproductive Technique on Newborns. Austin J In Vitro Fertili. 2014;1(2): 1010.

following ART compared with non-ART singletons show increases in LBW, preterm birth, small for gestational age, and birth defects. Although there have been small reductions in recent studies, but these morbidities are still higher for ART singletons. These increased risks are Multifactorial and related both ART procedures and underlying infertility. These causes may be parental characteristics and higher maternal age, with more being nulliparous. Extended embryo culture may increase the risk for preterm delivery. Also there is a greater risk of perinatal morbidity, and in particular a greater incidence of LBW, in children conceived with a fresh embryo transfer compared with that of a frozen embryo transfer [2,14-24]. The association of IVF with longer term clinical events has not been fully resolved but also the in-vitro techniques, the controlled ovarian stimulation, culture media, and possibly additional freezing or vitrification procedures seem to play a role. For example outcomes appear better for frozen-thawed compared with fresh embryo transfers, but are poorer than for non-ART infants. In addition to there is a concerning increase in large for gestational age infants born following frozen-thawed embryo transfer and limited data on the effects of embryo vitrification used instead of slow-freezing techniques.

Long-term outcome

The risk of developing cerebral palsy is nearly doubled and the risk of developing epilepsy is also higher. Behavioral problems including attention deficit/hyperactivity disorder may be more common in children born following ART than among naturally conceived children but the finding is uncertain. Data on autism are difficult to interpret. There may exist a small increase in the incidence of childhood cancer and there is greater evidence of an elevated risk of asthma [23]. To some extent, these risks are mediated by neonatal complications including prematurity and low birth weight but some effects such as cerebral palsy are likely to be linked to the increased rate of multiple births after ART. Many of the neonatal complications after ART are most likely linked to parental sub fertility and are less an effect of the ART technology [3-24].

Genetic problems

The possibility exists that imprinting errors, associated with sub fertility and/or ART, may result in long-term morbidity. Several studies have found that children born after ICSI have a small increased risk of both inherent and de-novo chromosomal abnormalities [16,24]. The risk of congenital malformations among children born after ICSI is similar to that for IVF children [16,24]. Excess structural chromosomal anomalies, cystic fibrosis micro deletions of the Y-chromosome and rare imprinting disorders associated with male infertility have been found in both male and female partners undergoing infertility treatment, and these risk direct transmission to offspring. Increased risks of structural birth defects are such as cardiovascular, musculoskeletal, gastrointestinal, urogenital birth defects in ART [18,24].

Conclusion

Even though the association of IVF with longer term clinical events has not been fully resolved, the causes of infertility, the *in vitro* techniques, the controlled ovarian stimulation, culture media, and possibly additional freezing or vitrification procedures seem to play a role. These increased risks are Multifactorial and related both ART procedures and underlying infertility. Therefore there have to be investigate risks of individual birth defects and disentangle the inter-related effects of different types of infertility and the multiple aspects of ART and the effect of ART procedures and underlying infertility on perinatal mortality and morbidity and on long-term outcome of babies.

References

1. Sunderam S, Kissin DM, Flowers L, Anderson JE, Folger SG, Jamieson DJ, et al. Centers for Disease Control and Prevention (CDC). Assisted reproductive technology surveillance--United States, 2009. MMWR Surveill Summ. 2012; 61: 1-23.
2. Schieve LA, Meikle SF, Ferre C, Peterson HB, Jeng G, Wilcox LS. Low and very low birth weight in infants conceived with use of assisted reproductive technology. N Engl J Med. 2002; 346: 731-737.
3. Helmerhorst FM, Perquin DA, Donker D, Keirse MJ. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. BMJ. 2004; 328: 261.
4. Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. Obstet Gynecol. 2004; 103: 551-563.
5. Basso O, Baird DD. Infertility and preterm delivery, birthweight, and Caesarean section: a study within the Danish National Birth Cohort. Hum Reprod. 2003; 18: 2478-2484.
6. 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: 485-503.
7. Pinborg A, Wennerholm UB, Thurin-Kjellberg A, Loft A, Aittomaki K, Söderström- 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: 87-104.
8. Sazonova A, Källen K, Thurin-Kjellberg A, Wennerholm UB, Bergh C. Factors affecting obstetric outcome of singletons born after IVF. Hum Reprod. 2011; 26: 2878-2886.
9. Confidential Enquiry into Maternal and Child Health. Perinatal Mortality 2007: United Kingdom. London: CEMACH; 2009.
10. National Institute for Health and Care Excellence. Clinical guideline 156. Fertility e assessment and treatment for people with fertility problems. 2013.
11. SR Murray, JE Norman. Multiple pregnancies following assisted reproductive technologies. A happy consequence or double trouble? Semin Fetal Neonatal Med. 2014; 19: 222-227.
12. Pandian Z, Templeton A, Serour G, Bhattacharya S. Number of embryos for transfer after IVF and ICSI: a Cochrane review. Hum Reprod. 2005; 20: 2681-2687.
13. Ban Frangez H, Korosec S, Verdenik I, Kotar V, Kladnik U, Vrtacnik Bokal E. Preterm delivery risk factors in singletons born after in vitro fertilization procedures. Eur J Obstet Gynecol Reprod Biol. 2014; 176: 183-186.
14. Rizwan N, Abbasi RM, Mughal R. Maternal morbidity and perinatal outcome with twin pregnancy. J Ayub Med Coll Abbottabad. 2010; 22: 105-107.
15. Raatikainen K, Kuivasaari-Pirinen P, Hippelainen M, Heinonen S. Comparison of the pregnancy outcomes of subfertile women after infertility treatmentand in naturally conceived pregnancies. Hum Reprod 2012;27:1162-1169.
16. Hansen M, Bower C. The impact of assisted reproductive technologies on intra-uterinegrowth and birth defects in singletons. Semin Fetal Neonatal Med. 2014; 19: 228-233.
17. Turkish Neonatal Society study group on Assisted Reproductive Techniques and Multiple Pregnancies. Neonatal outcomes assisted reproduction and multiple pregnancies. ÇocukSagligiveHastaliklariDergisi. 2010; 53: 258-266.
18. Konstantinidis G, Spasojevic S, Kostic Todorovic M. Newborns from in vitro

fertilization conceived pregnancies. J Matern Fetal Neonatal Med. 2010; 23: 110-112.

19. Morcel K, Lavoué V, Beuchée A, Le Lannou D, Poulain P, PladysP. Perinatal morbidity and mortality in twin pregnancies with dichorionic placentas following assisted reproductive techniques or ovarian induction alone: a comparative study. Eur J ObstetGynecolReprod Biol. 2010;153:138-42.

20. Black M, Bhattacharya S. Epidemiology of multiple pregnancy and the effect of assisted conception. Semin Fetal Neonatal Med. 2010; 15: 306-312.

21. Spasojevic S, Konstantinidis G, Doronjski A. [Morbidity and mortality of premature neonates after introduction of national in vitro fertilisation programme--our experience]. Srp Arh Celok Lek. 2010; 138: 67-71.

22. Tandberg A, Bjorge T, Nygard O, Børdahl PE, Skjaerven R. Trends in incidence and mortality for triplets in Norway 1967-2006: the influence of assisted reproductive technologies. BJOG. 2010; 117: 667-675.

23. Kallen B. The risk of neurodisability and other long-term outcomes for infants born following ART. Semin Fetal Neonatal Med. 2014; 19: 239-244.

24. Kurinczuk JJ, Bhattacharya S. Rare chromosomal, genetic, and epigenetic-related risks associated with infertility treatment. Semin Fetal Neonatal Med. 2014; 19: 250-253.

Austin J In Vitro Fertili - Volume 1 Issue 2 - 2014
ISSN : 2471-0628 | www.austinpublishinggroup.com

Citation: Türker G. The Effect Postnatal and Long-Term Outcome of Assisted Reproductive Technique on Newborns. Austin J In Vitro Fertili. 2014;1(2): 1010.