

The Increased Incidence of Preterm Birth and Low Birth Weight in IVF Children Following Double Embryo Transfers

Madeleine Ota

Academy of Our Lady of Peace

Objective

In vitro fertilization (IVF) is an assisted reproductive procedure that accounts for 1% of children in the United States. Although the number of embryo implantations varies with patients, currently, it is common practice for doctors to implant multiple embryos in a woman's uterus. This poster will evaluate to what extent double embryo transfer (DET) increases the incidence of preterm birth and low birth weight over single embryo transfer (SET).



Figure 1: Ultrasound of an IVF Embryo Transfer. A catheter is inserted into the middle of the uterine cavity, where it delivers the embryos suspended in a fluid. Retrieved from: <http://www.advancedfertility.com/eggdonor.htm>

Abstract

The average women between thirty-five and forty years of age will have to undergo up to five cycles of in vitro fertilization (IVF) for an embryo to successfully implant.⁵ Due to the high cost of IVF, 75% of women prefer to undergo double embryo transfer (DET), rather than single embryo transfer (SET), in order to minimize the number of cycles performed.⁴ Although DET raises the probability of becoming pregnant, it also increases the risk of preterm birth (PTB) as a result of multiple births even beyond the increased rate of PTB associated with IVF. In order to evaluate how much DET increases the risk of PTB, data was collected from several studies dealing with the correlation between the number of embryo implantations and PTB and low birth weight (LBW). SET had a lower risk of PTB than DET with a relative risk of 0.37, due to the reduced number of twins born.¹ More than half of naturally conceived twins have PTB, and twins conceived through IVF are 1.23 times more likely to have PTB and have a mean birth weight of 105 g below average twins' birth weights.³ Studies also showed that SET babies have a slightly higher rate of PTB than spontaneously conceived singletons. The relative risk is 1.84 with a mean body weight 97 g below average.² PTB and LBW make a baby susceptible to long-term problems, such as cerebral palsy, blindness, deafness, coordination disorder, and attention deficit hyperactivity disorder.⁶ Overall, embryo transfer through IVF contributes to the likelihood of PTB in both SET and DET over naturally conceived births. DET raises the risk even higher due to the increased risk of twins. The incidence of PTB stresses the need for women who wish to implant multiple embryos to be aware of the potential and the consequences of PTB and LBW.

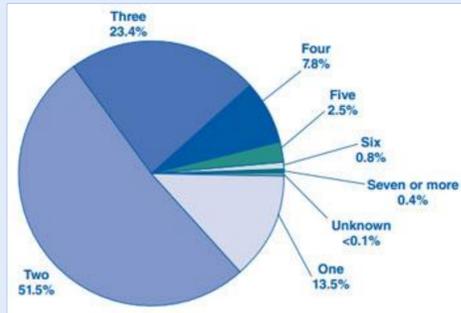


Figure 2: Percentages of Women with Single and Multiple Embryo Transfers. 75% of women opt for DET; however, studies from 2009 show that more than 80% end up implanting more than one embryo. Retrieved from: <http://singularityhub.com/2012/07/12/test-tube-babies-reach-major-milestone-5-million-born-since-1987/>

Methodology

Medline (1978-March 21, 2011) and Embase (1980-March 21, 2011) were searched for articles that examined perinatal mortality, PTB, and LBW in infants conceived by SET, DET/multiple embryo transfer (MET), or by natural conception. Out of 194 articles selected for full-review, only 15 met the criteria. 8 random control tests (RCTs) included 1,012 SET gestations and 1,064 DET. 8 observational studies (4 retrospective cohort studies and 4 prospective cohort studies) also met the criteria. They included 998 gestations from SET, 1,111 from DET, 57 from MET, and 74,842 spontaneously conceived singletons. Raw data was collected using a data collection form and was review by a perinatologist. All data came from developed countries, mainly from European research centers. Statistical analysis was performed by the Review Manager software. Dichotomous data was meta-analyzed with relative risk (RR) using a random effect model.

Results

Outcome	No. of Studies	No. of SET infants with outcome/total no. of SET infants	No. of control infants with outcome/total no. of control infants	Pooled outcome (95% CI), crude data
Perinatal mortality	2	1/141	2/199	RR 0.74 (0.09-5.94)
PTB (< 37 weeks)	4	27/388	96/446	RR 0.37 (0.25-0.55)
LBW (< 2,500 g)	3	13/183	72/247	RR 0.25 (0.15-0.45)

Figure 3: Outcomes of the Meta-analysis of the RCTs of SET Compared with DET. The table demonstrates the relative risk (RR) a SET infant has of being affected by one of the specified outcomes. Adopted from tables by: Alavi, N., Grady, R., Khandwala, M., McDonald, S., & Vale, R. (2012).

Outcome	No. of Studies	No. of SET infants with outcome/total no. of SET infants	No. of control infants with outcome/total no. of control infants	Pooled outcome (95% CI), crude data
PTB (<37 wk)	2	58/520	4,335/74,572	RR 2.13 (1.26-3.61)
LBW (<2,500 g)	2	27/520	3,396/74,572	RR 1.46 (0.91-2.33)

Figure 4: Outcomes of the Meta-analysis of SET Compared with Spontaneously Conceived Singletons. The table above shows the relative risk (RR) for a SET infant, compared with that of a naturally conceived singleton, of being affected by either of the specified outcomes. Adopted from tables by: Alavi, N., Grady, R., Khandwala, M., McDonald, S., & Vale, R. (2012).

The data showed that DET infants had a greater risk of the study's specified outcomes (perinatal mortality, PTB, and LBW) than SET infants. 4 random control tests (RCTs) found that 27 out of 388 (-6.96%) SET pregnancies had PTB (less than 37 weeks gestation), compared to the 96 out of 446 (-21.52%) DET pregnancies that had PTB. The RR of PTB in SET children versus DET children was calculated to be 0.37. In addition, 3 RCTs demonstrated that 13 out of 183 (-7.10%) SET babies had a LBW (less than 2,500 g), compared to 72 out of 247 (-29.15%) DET babies with LBW. The RR for LBW in SET children versus DET children was 0.25. The study also tested for a difference in the incidence of PTB and LBW in SET infants and spontaneously, or naturally conceived, singletons. The data collected showed that SET infants had an increased incidence of the outcomes than spontaneously conceived singletons. The RR for PTB in SET infants compared to spontaneously conceived singletons was calculated to be 2.13. The RR for LBW in SET infants compared to spontaneously conceived singletons was 1.46.

Discussion

In comparing SET infants to spontaneously conceived singletons, data shows that the risk of PTB and LBW is increased in IVF babies. Although the reasons are still unclear, it can be deduced that IVF influences the occurrence of these two outcomes. The risk of PTB and LBW is further raised by the DET procedure. Multiple births is a likely cause of the increased rate of PTB and LBW in DET infants, since more than half of twins are born premature. Many women in the U.S. rely on DET to decrease the number of IVF cycles they need to undergo. The average cost of an IVF cycle in the U.S. is over \$12,000, more than twice the cost in most other countries. With the increased number of DET procedures (and even multiple embryo transfers) there is a greater incidence of PTB and LBW in IVF babies. Because these outcomes can cause problems in a child's physical and cognitive development, DET raises the ethical debate over whether or not it is morally right to put a patient's desire for children above the health of his/her potential child(ren). Regardless of ethics, it is crucial that the patient is aware of the potential risks involved in IVF and DET, so that she can decide whether or not the risks outweigh the benefits.

Applications to Biotechnology

Since 1978, IVF has helped millions of infertile people have children. Although IVF gives life to so many families, it is necessary to understand how IVF effects children. It is still unclear of why the IVF procedure itself causes PTB and LBW. Only further research can reveal these causes and hopefully work to eliminate them for future patients. For now, it is evident that DET increases the risk of PTB and LBW. Implanting one embryo could not only benefit future IVF children, but also the economic community, since the cost of preterm baby care has the potential of outweighing the cost of an IVF cycle.

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