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Editorial

Risks Associated with Assisted Reproduction Technology – How Much Do the Medical Profession and Lay Public Know?

V Y H Yu

Since the first in vitro fertilisation (IVF) birth exactly 20 years ago, more than 20,000 children are currently being born annually around the world from assisted reproduction technology. In Australia, we have more than 2,800 such births every year, representing 1% of all births within the country. It is now apparent that these procedures increase the risk of multiple pregnancy, prematurity and low birthweight which have serious consequences on perinatal mortality rate and cerebral palsy. It is of concern that the medical profession and lay public might not be fully aware of the adverse medical, social and economic outcomes of IVF pregnancies.

In spite of an encouraging decline in the number of embryos transferred in IVF procedures carried out in Australia, it was reported that nationally in 1995, more than three embryos were transferred in 2% of IVF cycles⁽¹⁾. Twins occurred in 15%, triplets in 1.5% and quadruplets in 0.1% of IVF pregnancies. The risk of multiple pregnancy increases with the number of embryos transferred: it was noted that twinning increased from 13% after the transfer of two embryos to 20% after three embryos to 23% after four embryos.

IVF pregnancies have poorer than normal outcome with regards to spontaneous abortion (21%), ectopic pregnancy (5%), preterm birth (21%) and low birthweight (24%). The prematurity and low birthweight rates in IVF pregnancies were higher with increasing plurality (Table I), but even among singleton IVF pregnancies, the prematurity rate of 13% and the low birthweight rate of 10% were double that for all Australian pregnancies.

Our national fetal, neonatal and perinatal mortality rates of IVF pregnancies (Table II) were six times higher than that for all Australian births. This is due to a greater proportion of preterm and low birthweight infants, many of whom were multiple births.

Compared to a control population, more IVF infants have been reported to experience neonatal problems (45% versus 8%), the most common of which are respiratory distress, sepsis, jaundice and feeding difficulties⁽²⁾. IVF infants from multiple

Table I – Prematurity and low birthweight in singleton and multiple IVF pregnancies

	Singleton	Twins	Triplets	All IVF*
Gestation (weeks)				
< 27	28 (2.0%)	15 (5.8%)	5 (18.5%)	48 (2.8%)
< 32	47 (3.4%)	35 (13.6%)	13 (48.1%)	96 (5.6%)
< 36	181 (12.9%)	143 (55.9%)	27 (100%)	352 (20.9%)
Birthweight (grams)				
< 1,000	26 (1.8%)	30 (5.8%)	16 (19.8%)	72 (3.6%)
< 1,500	37 (2.6%)	70 (13.7%)	42 (51.9%)	153 (7.6%)
< 2,500	134 (9.5%)	260 (50.8%)	76 (93.8%)	474 (23.7%)

* included one quadruplet pregnancy

Table II – Fetal, neonatal and perinatal mortality rates (per 1,000) in IVF pregnancies

	Singleton	Twins	Triplets	All IVF
Fetal mortality	19	39	62	26
Neonatal mortality rate	6	31	79	15
Perinatal mortality rate	25	68	136	40

births have a higher proportion of neonatal disorders compared with singletons (69% versus 25%). IVF infants are more likely to require assisted ventilation and use more ventilator bed days compared with non-IVF infants. They were reported to account for 5% of total ventilator days in a Neonatal Intensive Care Unit⁽³⁾. Although this could be partly explained by preterm delivery and multiple pregnancies, even singleton IVF infants use more ventilator bed days than non-IVF infants. At 4 years of age, neurodevelopmental disabilities have been reported in 2.1% of IVF children (all from multiple births) compared to 0.4% in controls⁽²⁾.

IVF results in adverse perinatal outcome primarily because it increases the risk of multiple pregnancy and thus preterm birth. However, even singleton IVF pregnancies have a higher prematurity rate than expected. Other studies have suggested that this risk of preterm birth is higher when more embryos are used to achieve the singleton pregnancy⁽⁴⁾.

Australia has made a serious effort to reduce the number of embryos implanted in any one cycle. Evidence is lacking that the transfer of more than two embryos improves pregnancy rates⁽⁴⁾. Although selective reduction of fetuses had been performed in early pregnancy to abort a severely malformed fetus in a multiple pregnancy or to avoid multiple births, there is no evidence that this procedure reduces obstetric or perinatal problems⁽⁵⁾. Fetal reduction is therefore not a solution and one should aim to avoid a multifetal pregnancy at the time when IVF is performed. Guidelines published by most national IVF committees recommend that no more than three embryos be transferred in any one cycle. However, in view of the adverse perinatal consequences of triplets and the lack of benefit in improving pregnancy rates with the transfer of three or more embryos, it is advisable that the number of embryos transferred be restricted to no more than two per cycle in order to reduce the risks of multiple birth and prematurity.

It is uncertain how often the infertile couple considering IVF is aware of the significantly higher risks of adverse perinatal outcome and the possibility of substituting an infertility problem with the problem of having to face the responsibility for the life-long care of a child or children with cerebral palsy. There are moral and medico-legal obligations to provide counselling on the consequences of multiple birth and prematurity associated with IVF. Perhaps, the transfer of only single embryo especially on the first treatment cycle, should be considered as a serious option. A national audit of all IVF units is vital. The success rate of an IVF unit should be measured by adding up the number of singleton healthy term delivered, and subtracting from it a score of two, three or four for twins, triplets or quadruplets.

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