in a longer perspective that is not at all true.

2. Q: Do multiples save time for the couple to achieve their reproductive goal for a larger family?
A: Only marginally so. And it saves quality of life for children and families alike.

So, all evidence available on 
a/ medical risks,
b/ psycho-social problems,
c/ economy and 
d/ feasibility for effectiveness 
all speak the same language: A shift in clinical policy to avoid, totally, high order of multiple pregnancy (triplets or more) and to decrease the proportion of twins is logical, rational and beneficial to all parties involved.

REFERENCES


Karl Nygren, MD
IVF-clinic at Sophiahemmet Hospital, Stockholm, Sweden.

Comment by:  Ragaa Mansour, M.D. Ph.D
Cairo, Egypt

Women undergoing in vitro fertilization (IVF) have been shown to have a higher percentage of twin, triplet and even higher order deliveries than their non-IVF counterparts. This has even been estimated to reach as high as a 20-fold increased risk of twins and a 400-fold increased risk of high order pregnancies (1). ART surveillance on multiple pregnancy rates in the USA, for the years 2000 and 2001, demonstrated that the twin deliveries rates were 44% and 46%, respectively (2, 3). In addition, the triplet and higher deliveries rate were 9% and 8% respectively. Also, the European ART registry for the same years reported twin deliveries rates at 24.4% and 24% and the triplet delivery rates at 2% and 1.5% respectively (4, 5). Furthermore, the Middle East IVF registry for the year 2000 (6) reported a twin deliveries rate of 27% and triplet and higher deliveries rate of 5%

It has been well recognized that multiple pregnancy is associated with an increased risk of maternal and perinatal morbidity and mortality (7 - 9). Preventative measures to reduce the multiple pregnancy rate include: a) soft ovulation induction, b) reducing the number of embryos per embryo transfer, c) optimizing embryo cryopreservation, and d) secondary prevention by multifetal pregnancy reduction as a back-up procedure. One of the most important factors affecting the multiple delivery rates is the number of embryos transferred per cycle. Most European centers now have moved away from the traditional three-embryo to a new two-embryo transfer policy. Consequently, triplet rates have fallen, however, the twin rates still remain almost unchanged (4).

In the USA, from 1995 to 2001, the average number of embryos per transfer began decreasing in 1997, with an 11% decrease between 1998 and 1999. In contrast, the number of live birth per cycle has steadily increased. Furthermore, even though the rate of twin pregnancies did not change significantly, the multiple pregnancy rates with three or more has significantly decreased; with a marked decline of 20.8% between 1998 and 1999 (10).

The residual problem is how to decrease this high rate of twin pregnancies (25 - 45%). Obviously, a strategy using single embryo transfer would eliminate the problem of a high twin pregnancy rate. Even though, some important questions still remain to be answered about the single embryo transfer before it becomes the standard: a) Will it lower the overall birth rate? b) Who is at a significant risk for twin pregnancy? c) What are the definite criteria to select the best embryo? d)
Are the cryopreservation standards uniform, and successful? e) Is the patient going to bear the costs of IVF treatment?

Gerris et al., (11) conducted a two-center prospective, randomized controlled trial to compare the results of single vs. double embryo transfers. They found that the live birth rate between the SET and DET groups were similar (37.4 and 36.6% respectively). Even though the percentage of prematurity (8.5 and 23.8%, respectively) and neonates requiring hospitalization was higher in the DET group (5.7% and 17.9%, respectively). Moreover the total cost of SET was almost one-half that of DET (4700 + 3239 vs. 8613 + 1015). This prospective health economic study shows that the transfer of a single top quality embryo is equally effective as, but substantially cheaper than, double embryo transfer in women < 38 years of age in their first IVF / ICSI cycle.

In a second multi-center prospective, randomized controlled trial to compare the results of elective single vs. double embryo transfers, Thurin et al. (12) found that the cumulative pregnancy and live birth rates were similar between the two groups, the multiple birth rates were significantly lower in the SET group. However, the fresh pregnancy and live birth rates were significantly higher in the double embryo transfer (33.6% and 27.6% vs. 52.6% and 42.9%). They concluded that in women less than 36 years of age, transferring one fresh embryo and then, if needed one frozen and thawed embryo, dramatically reduced the rate of multiple births. Furthermore, The rate of cumulative live birth was not substantially lower than with the double-embryo transfer group.

In addition, a recent Cochrane review illustrated that the live birth and pregnancy rates following SET are lower than those following DET, but also are the chances of multiple pregnancies, including twins (13). Furthermore, in a prospectively, randomized trial, Marieke Lukassen et al., (14) compared the effect of two cycles with single embryo transfer versus one cycle with double embryo transfer. The aim was to calculate the cost effectiveness of both strategies. The study included 107 women aged <35 years, in their first IVF cycle. The results showed that the cumulative live birth rate per woman randomized was non-significant between the two groups, but the resulting multiple pregnancy rates were significantly higher in the double embryo transfer arm (0% vs. 37%). In addition, they inferred that two cycles with SET were equally effective as one cycle with DET. Furthermore, the medical costs per live birth up to 6 weeks after delivery were noted to be relatively the same. However, if lifetime costs for severe handicaps are included, more than 7,000 per live birth will be saved after implementing SET. Because of the high probability of multiple pregnancies in patients <35 year and in their first IVF cycle, only SET should be performed (14).

Finally, a systematic review on single embryo transfer identified four RCT and seven observational studies (15). The pooled results of the four RCT showed that the combined pregnancy rate for the SET and DET were 31.3 and 48.1% respectively. In addition, the delivery rate was 28 and 42.4% respectively, and the twin rate was only 2% in the SET, but was 34.9% in the DET group. In the seven observational studies, the pooled pregnancy rate for the SET and DET were 33.8 and 43.3% respectively. In addition, the delivery rate was 29.2 and 28.2% respectively. Lastly the twin rate was 1% in the SET, but was 31.4% in the DET group.

The authors concluded that SET could result in a satisfactory delivery rate in good prognosis patients. However, the overall delivery rate was significantly lower after SET compared to DET, but might be restored with the cumulative effect of frozen-thawed embryo transfers. Even though, it is important to note that there was also a dramatic decrease in multiple birth rate resulting from SET (15). Moreover, the observational studies indicated that SET and DET could achieve similar pregnancy and delivery rates, and SET substantially decreased the multiple pregnancy rates. However, the two groups were not strictly comparable (15).

In summary, multiple pregnancies are an iatrogenic epidemic complication as a result of ART. All measures have to be taken to prevent it. Single embryo transfer is one of the most effective measures for the prevention of multiple pregnancies. However, the current evidence is not enough to initiate a change in clinical practice. Financial issues have to be taken into consideration.
Clinicians may need to individualize protocols for couples based on their risks of multiple pregnancies. Furthermore, cryopreservation protocols have to be optimized and standardized.

REFERENCES

Ragaa Mansour, M.D. Ph.D.
Director,
The Egyptian IVF-ET Center

Comment by: Raja Al-Karaki, M.D.
Amman, Jordan

Introduction
The progress in assisted reproduction technologies over the last 25 years has led to a tremendous success in obtaining pregnancies and deliveries in different categories of infertility. The success of these technologies should not be judged by only achieving a pregnancy but what has to be taken into consideration is the safe obstetrical and neonatal outcomes with the objective of the delivery of healthy baby which gives true reflection of a successful practice. The main factor in IVF programme increasing obstetrical and perinatal risks is the high rate of multiple pregnancies. This is due to the widely practiced policy of transferring more than one or two embryos in order to compensate for the low implantation rate and achieve higher pregnancy rate (PR) which may affect negatively the final outcome. It has been approved that multiple gestation carry several risks for both the fetuses and the mother. Maternal complications are mainly pregnancy induced hypertension, preterm labor, antepartum hemorrhage and surgical delivery. Adverse neonatal outcomes involve preterm birth, low weight and