



CLINICAL OPINION

The decreased rates of triplet births: Temporal trends and biologic speculations

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KEY WORDS

Multiple birth Twins Triplets ART Embryo transfer Recent data from the US and from England and Wales demonstrate decreasing rates of higher-order multiple births and represent, for the first time, a striking change in trend when compared with the previous steep 4-fold increase since the early 1980s. However, the incidence of other multiples—twins—continued to escalate. The most probable reasons for this change are new embryo transfer guidelines and availability of multifetal pregnancy reduction procedures. Because actual numbers of higher-order multiples are by far lower than the number of twins, and because twins are predictably associated with significant perinatal morbidity and mortality, the implications of the ever-increasing multiple birth rates are no less alarming. As long as the incidence of twins is not reduced, the decreasing incidence of higher-order multiples, per se, does not herald the end of the epidemic of multiple births.

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Multiple pregnancies are disadvantaged compared with singleton gestations in terms of perinatal morbidity and mortality, as the potential for adverse perinatal outcomes increases with increasing plurality. Because of the increased incidence of multiples, and because triplets comprise the majority of higher-order multiples, the impact of triplets on perinatal outcomes is of primary concern. The dramatic increase in the triplet birth rate is commonly characterized as being of 'epidemic proportions,' and is attributed to assisted conceptions, including the use of potent ovulation enhancing drugs as well as assisted reproductive technologies (ART). A recent study of triplets and higher-

order multiple births found that 43% result from ART, 40% are likely the result of non-ART treatments, and only 18% were spontaneous pregnancies. Data from the Belgian population-based East Flanders Prospective Twin Study suggest that within that obstetric population, 30% of triplets resulted from ART, 52% from ovulation induction treatment, and only 18% were spontaneous triplet conceptions.

Public health concerns related to the much-increased incidence of higher-order multiples are not new. As early as the late 1980s, when high-order multiples were recognized as a serious side effect of infertility treatment, 2 principal measures to diminish their occurrence were proposed: multifetal pregnancy reduction (MFPR), and decreasing the likelihood of multiple ovulation and number of transferred embryos in assisted conceptions.

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Whereas the former, primarily a 'curative' measure, may decrease the number of multiple births, the latter—primarily a preventive measure—may decrease the number of multiple pregnancies. Although prevention is always considered better than cure, both measures have not been implemented to the same extent. As a result, the efforts to improve MFPR techniques preceded efforts to improve implantation rates in in vitro fertilization. Regardless, the incidence of triplets continued to escalate in the late 1990s in most developed countries.

The light at the end of the tunnel was reported in the US in the annual vital statistics of 2002. According to this report, twin birth rate has continued its steady increase since 1981, rising 3% for 2002 to 31.1 per 1000 total live births, representing an increased twinning rate of 38% since 1990, and 65% since 1980 (18.9 per 1000 total live births). On the other hand, the 2002 rate of triplet and higher-order multiple births decreased slightly (1%), from 185.6 to 184 per 100,000 births, continuing a small (5%), but steady decline observed since 1999. This change in trend is particularly striking when compared with the previous steep increase of more than 400% (from 37.0 to 193.5 per 100,000 live births), with an average annual increase of 13% between 1980 and 1998.

Even more striking are the changes in rates of higherorder multiple births observed in England and Wales (Figure). The trend line for twins indicates a steady and continuing increase, from 9.95 to 14.47 per 1000 live births during the period 1982 to 2002 (48% increase, with an average annual increase of 2.3% between 1982 and 2002). In contrast, triplet births increased 400%, from 0.12 to 0.48 per 1000 live births until 1998, when a definite turning point in the trend line became evident. In 1999, however, the rate of triplet births decreased 37.5% in the following years, from 0.48 to 0.3 per 1000 live births (Figure).

This paper discusses some unanswered questions related to these changes in triplet births.

Does the change in trend represent the end of the triplets epidemic?

Obviously, an apparent change in trend, even when observed over a period of several years, does not conclusively represent the actual end of the escalating numbers. The English and Welsh data indicate that the 2002 figures of triplet births are still 250% higher than background rates, ie, figures observed during the early 1980s, before the era of assisted conceptions. The US data are far less encouraging in the sense that they, at best, represent plateauing of the rates, rather than a real decline.

Having said this, 2 points should nonetheless be acknowledged. First, in terms of the 'epidemic' of triplet births, these changes in patterns of birth rates may, after all, correspond to the extent of the ability of our

profession to control the epidemic. Second, if past trends are used to extrapolate future trends, ¹¹ these turn points may indeed herald a real decrease in the rate of triplets. Regardless, from the perspective of health care, any (negative) change in the escalating rates of triplet should be welcomed. At present, any further assumption must await birth data for the next several years.

What caused the change?

At present, we are unable to identify which factor does play the most important role in decreasing the rates of triplets. However, several potential explanations may affect the decrease or plateau in the triplet birth rates. First, and least plausible, is that it represents a decline in infertility treatments, hence a decline in the number of higher-order multiple pregnancies. This explanation can be discarded from the outset because data show a 33% increase in ART procedures reported to the Centers for Disease Control and Prevention from medical centers in the US during the period 1998 to 2001. 12,13 The second explanation is that the 1999 guidelines issued by the American College of Obstetricians and Gynecologists and the American Society of Reproductive Medicine, ¹⁴ in addition to improved outcomes of ART, lowered the number of transferred embryos, hence, reducing the triplet birth rates. A recent matching between outcomes of ART procedures and rates of twin and triplet or higherorder multiple births found that from 1995 to 2001 in the US, the average number of embryos transferred per cycle began decreasing in 1997, with the steepest decline (11.1%) between 1998 and 1999. 13 Although the twins birth rates did not change significantly between 1997 and 2001, the rate of triplets and higher-order multiple births significantly decreased every year, with the steepest decline (a 20.8% decrease) between 1998 and 1999, after the publication in 1998 of the American Society for Reproductive Medicine guidelines for embryo transfer. 14

A less clear cause and effect relationship between treatment guidelines and triplet rates is seen in the UK. The previous (2001) code of practice in the UK permitted the transfer of 3 embryos, but only in exceptional cases. The consequences of this vague guideline were that infertility centers continued to transfer 3 embryos in many women. Data collected in 2000 in the UK show that 3 embryos were transferred in as many as one third of all IVF cycles, and 58% of cycles used 2 embryos. It follows that the decline in triplet rates shown in Figure, starting at 1998, preceded the UK recommendations for embryo transfers and, therefore, the association between embryo transfer policy and triplet rates is not clear cut. Obviously, the effects of implementing the newest (January 2004) guidelines ¹⁶ are not represented in this Figure.

A third explanation is a decrease in the number of ovulation induction procedures and an increase in the

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