Fecundity and twinning. A study within the Danish National Birth Cohort

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BACKGROUND. Decreased fecundity has been hypothesized as one of the causes of the widespread decline in twin rates in the 1960s and 1970s. The association between high fecundity and twinning is not, however, well documented. METHODS. In the Danish National Birth Cohort, we identified 56,295 births (including 729 twin deliveries) with data on pregnancy planning and time to pregnancy (TTP) and no report of infertility treatment. We estimated the odds ratio (OR) of twinning as a function of TTP and having planned a pregnancy. RESULTS. Increasing TTP correlated with decreased twinning rates. Compared with women who conceived within 2 months of trying, women who took longer than 1 year had an OR of 0.55 (95% confidence interval 0.39–0.77) of giving birth to twins. The association was slightly stronger for opposite sex twins. Women not planning a pregnancy had a lower rate of opposite sex twins than planners, but a comparable rate of same sex twins. We saw an excess of same sex pairs in women conceiving despite contraception. CONCLUSIONS. A long TTP is associated with a reduced risk of twinning. The marked decline observed in the 1960s and 1970s may derive from a widespread decrease in fecundity.

Key words: fecundity/time to pregnancy/twinning

Introduction

Twinning rates declined in many countries from the 1950s through most of the 1970s (Rachootin and Olsen, 1980; James, 1982, 1986; Doherty, 1988; Tong and Short, 1998; Astolfi et al., 2003). The decrease, reportedly in the estimated fraction of dizygotic (DZ) twins, has been one of the most profound unexplained changes in human reproduction.

‘Natural’ twinning is considered a marker of high fecundity, as it involves a double ovulation, successful fertilization of two ova, and maintaining a multiple pregnancy up to the time of delivery (Lazar et al., 1977), but this association has only been documented indirectly. Bulmer (1959) reported that, among legitimate births, more twins appeared to be conceived in the first 3 months of marriage compared with successive periods. Eriksson and Fellman (1967) reported high twinning rates in illegitimate births in the Scandinavian countries in different time periods, and suggested that women giving birth to illegitimate babies may have a higher fecundity. Allen and Shachter (1971) investigated the variation in twinning and birth rates in the USA in 1946, when soldiers were returning from the Second World War, and estimated that the increase in twin conceptions preceded by 2.2 months the increase in singleton births. Philippe and Roy (1989) examined the interval to first births in mothers of singletons and mothers of twins, and their results suggested that mothers prone to having opposite sex twins could have higher fecundity than mothers of singletons.

From the 1980s, multiple deliveries have been steadily increasing, most likely due to increasing use of ovarian-stimulating drugs and IVF (Westergaard et al., 1997; Tong and Short, 1998; Astolfi et al., 2003; Imaizumi, 2003). Some reports suggest, however, that the ‘natural’ twinning rate is also increasing, at least in younger women (James, 1998; Astolfi et al., 2003). If high fecundity is linked to twinning, the observed decline could signify that a widespread decrease in fecundity has occurred at some time in the recent past.

We used data from the Danish National Birth Cohort to explore for the first time the direct association between fecundity, as measured by time to pregnancy (TTP), and twinning.

Methods

Women were recruited to the Danish National Birth Cohort early in pregnancy. Depending on the participation of general practitioners, ~60% of eligible women were reached nationwide, and ~60% chose to participate (Olsen et al., 2001).

We linked 64,167 first interviews to 62,122 births identified through the Danish Hospital Registry and the National Birth Registry. We failed to link 345 live births that could not be found in the Birth Registry (possibly due to delays in registration, deliveries
In this analysis, we excluded 17 deliveries before 24 completed weeks, 9 stillbirths with no information on twinning status, and 23 sets of triplets. Since there were only a few such cases \((n = 61)\), we also excluded births for which information on parity or smoking during pregnancy was missing (as we used these covariates in the analysis). Women taking 6 months or longer to conceive were asked whether they had received infertility treatment, and we excluded the 3901 pregnancies where infertility treatment was reported. Of the 58111 pregnancies remaining, 1816 were by women contributing more than one pregnancy to the sample and, in this case, we kept the most recent. We thus had 56295 pregnancies for analysis, including 729 pairs of twins (1.3%). The births in this analysis occurred between March 1998 and December 2001, and the interviews had been administered between December 1997 and July 2001. The frequency of twin deliveries was 1.6% in 1998, 1.3% in 1999, and 1.2% in 2000 and 2001. In 1998, the cohort was recruited in only one region.

Women were asked whether their pregnancy had been planned. If the pregnancy was ‘planned’ or ‘partly planned’, participants were further asked ‘How long did you try to become pregnant before you succeeded?’ (possible answers were ‘did not try to become pregnant’, ‘became pregnant right away’, ‘1–2 months’, ‘3–5 months’, ‘6–12 months’, ‘more than 12 months’, ‘don’t know’, ‘do not wish to answer’). We grouped together women who reported conceiving right away and those taking 1–2 months. We first examined the association between TTP and twinning only among planners \((n = 41209)\), and we then compared planners with non-planners. Seventy percent of women reporting that their pregnancy was partly planned reported a TTP, but we considered them among non-planners nonetheless, since we were uncertain about the validity of the reported TTP. Women who said that their pregnancy was planned but did not report a TTP, either because they did not know it \((n = 71)\) or because they reported not trying to become pregnant \((n = 306)\), were categorized as part planners. However, we also estimated the association between TTP and twinning by including the TTP reported by the part planners and, additionally, attributing a TTP of up to 2 months to the 306 women who said that they had planned their pregnancy but had not tried to become pregnant. Fifteen women who did not answer the question on planning were considered as non-planners. As the outcome, we considered all twins first and then opposite sex twins. Same sex twins were excluded from this subanalysis. The sex of the twins was missing for nine pairs (due to stillbirth of one or both of the babies), which were excluded from the analyses where the sex of the pair was relevant. However, we kept in the analyses singletons with missing sex.

We estimated odds ratios (ORs) of twinning as a function of TTP and planning using logistic regression models adjusted for mother’s age at delivery, parity, smoking and body mass index (BMI). The decision to include these factors was made a priori, based upon their known correlation with TTP. There were 994 cases in which BMI was missing, and we included a separate category in the model for these. All variables were categorized as reported in the footnote to Table I.

**Results**

Figure 1 illustrates the frequency, stratified by parity, of twin deliveries in (a) all women and (b) ‘young’ mothers as a function of TTP, among women who planned their pregnancy. We defined as ‘young’ primiparas aged 28 years or less and multiparas aged 31 or less, as these values represented the respective median ages at delivery. The trend between TTP and twinning for primiparas was not statistically significant \((P = 0.08)\) while that for multiparas was \((P < 0.001)\). The pattern was virtually unchanged when we restricted the analysis to young mothers. There was, however, no significant interaction between TTP and parity in relation to twinning, and we therefore present a common analysis.

Table I shows the association between TTP and twinning. Women who conceived within 2 months of trying had the highest frequency of twin deliveries, and the rate decreased
with increasing TTP. These results were slightly stronger for opposite sex twins. For young women taking 2 months or less to conceive, the OR associated with a TTP of longer than 12 months was 0.46 [95% confidence interval (CI) 0.26–0.81] for all twins. There were only 88 opposite sex twins. For young women taking 2 months or longer to conceive, the OR associated with a TTP of longer than 12 months was 0.46 [95% CI 0.73–1.11]. We examine this further in Table II.

When we added to the planners the 5547 part planners who reported a TTP, the association between TTP and twinning persisted but was slightly weaker, especially among women reporting a TTP of 6–12 months (OR = 0.70, 95% CI 0.55–0.89) and those reporting a TTP longer than 12 months (OR = 0.59, 95% CI 0.42–0.81). We saw a similar pattern when restricting the outcome to opposite sex twins (data not shown). When we further added the 306 women who had planned a pregnancy but had not reported a TTP (attributing to them the TTP of 0–2 months) because ‘they had not tried to become pregnant’, the results were virtually identical to those presented in Table I, both for all twins and for opposite sex twins (data not shown).

Compared with planners, women who had not planned a pregnancy had an OR of twinning of 0.78 (95% CI 0.66–0.93) when all twins were the outcome, and of 0.48 (95% CI 0.33–0.70) when opposite sex twins were the outcome. The OR of having same sex twins was, on the other hand, 0.90 (95% CI 0.73–1.11). We examine this further in Table II. The frequency of same sex twins was highest in the category of women who had conceived despite contraception, although this estimate is based on small numbers. The difference between the rates of same sex twins as a fraction of all twins across these categories was significant (P = 0.024).

### Discussion

Dizygotic twinning has been considered a measure of high fecundity for a long time, despite lack of direct evidence. In this study, we found that women conceiving within 2 months of trying had an 82% higher risk of giving birth to twins compared with women taking longer than 1 year.

When interpreting the results, it is important to consider that the question regarding having received infertility treatment was only asked of women who said that their pregnancy had been planned or partly planned (or failed to respond to that question) and who reported a TTP of 6 months or longer. It is possible that some women with a short TTP had also received treatment. This may bias our results, since treated women are more prone to twinning. For this mechanism to generate the trend we saw, however, there should have been more treated women among those with a waiting time of less than 2 months than among those with a waiting time of 3–5 months, which seems unlikely. While ~45% of the women taking longer than 12 months had reported treatment, only 7% reported treatment among those with a waiting time of 6–12 months, and we expect this fraction to be substantially lower in women with shorter waiting times. Furthermore, when we restricted the analysis to younger mothers, who would, overall, be less likely to have received treatment, we saw the same trend as in the whole sample.

Primiparas showed a peak in twinning among women taking longer than 1 year to conceive, which suggests that some may have failed to report infertility treatment. Part of the observed peak may be explained by the fact that these women were older (which increases the probability of twinning), since it was less pronounced when the analysis was

### Table I. Frequency of twin deliveries and adjusted ORs (95% CI) according to categories of TTP among women who planned their pregnancy

<table>
<thead>
<tr>
<th>TTP</th>
<th>All twins</th>
<th>Opposite sex twins</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Twins (%)</td>
</tr>
<tr>
<td>0–2 months</td>
<td>20,759</td>
<td>324 (1.59)</td>
</tr>
<tr>
<td>3–5 months</td>
<td>9584</td>
<td>134 (1.40)</td>
</tr>
<tr>
<td>6–12 months</td>
<td>6831</td>
<td>68 (1.00)</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>4035</td>
<td>37 (0.92)</td>
</tr>
</tbody>
</table>

Adjusted for mother’s age at delivery (≤25 years, 26–30, 31–35 and 36+), parity (no previous births, one previous birth, 2+ previous births), smoking in pregnancy (yes/no) and pre-pregnancy BMI (<20, 20–24.9, 25–29.9, 30+ and missing).

### Table II. Rate of same sex twin deliveries among planners and non-planners

<table>
<thead>
<tr>
<th>Planning</th>
<th>All births</th>
<th>All twins</th>
<th>SS twins</th>
<th>% SS/all births</th>
<th>Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planned</td>
<td>41,205</td>
<td>559</td>
<td>372</td>
<td>0.91</td>
<td>0.67 (0.62–0.70)</td>
</tr>
<tr>
<td>Unplanned (total)</td>
<td>15,081</td>
<td>161</td>
<td>129</td>
<td>0.86</td>
<td>0.80 (0.73–0.86)</td>
</tr>
<tr>
<td>Partly planned</td>
<td>7,949</td>
<td>88</td>
<td>69</td>
<td>0.87</td>
<td>0.78 (0.68–0.86)</td>
</tr>
<tr>
<td>Unplanned</td>
<td>5,367</td>
<td>50</td>
<td>39</td>
<td>0.73</td>
<td>0.78 (0.64–0.88)</td>
</tr>
<tr>
<td>Despite contraception</td>
<td>1,765</td>
<td>23</td>
<td>21</td>
<td>1.20</td>
<td>0.91 (0.72–0.99)</td>
</tr>
<tr>
<td>Total</td>
<td>56,286</td>
<td>720</td>
<td>501</td>
<td>0.90</td>
<td>0.70 (0.66–0.73)</td>
</tr>
</tbody>
</table>

*In this table, nine pairs of twins are omitted from all figures because of missing sex (four among planners and five among non-planners). SS = same sex pairs.
restricted to young mothers. However, since older primiparas are also more likely to receive infertility treatment, we cannot distinguish between these two explanations.

Although it had been reported that there was a higher proportion of twins among illegitimate births, at least in the past (Eriksson and Fellman, 1967; James, 1998), our data did not support this observation, reflecting recent findings in England and Wales (James, 1998). This is probably due to the current wide availability of contraception and the option of interrupting an unwanted pregnancy. Effective contraception and family planning would be likely to cause twin-prone women to lose their relative advantage over the less fecund, leading them to contribute fewer births to the total (Rachootin and Olsen, 1980; Doherty, 1988), and this may have been a factor in the observed decline of twin deliveries during the 1960s and 1970s.

Our results suggest that women who had become pregnant despite contraception gave birth to an excess of monozygotic twins, even though these estimates are based on very small numbers. Monozygotic twinning is reportedly associated with over-ripe (Witschi, 1952; Jakobovits and Iffy, 1988) and damaged oocytes (Hall, 2003). Women may be less rigorous in using contraception when they are convinced of being outside their fertile window, and our observation is consistent with a larger number of conceptions involving over-ripe oocytes among women conceiving despite contraception. The association between over-ripe oocytes and twinning was also reported for the dizygotic fraction of twins (Harlap et al., 1985), but our data did not support this observation.

Although the women in the cohort represent only about one-third of all eligible women, we do not think that this could have biased our findings concerning TTP among planners and twinning. To generate a spurious trend such as the one we saw, women would have had to participate in the cohort as a function of both length of TTP and twin pregnancy status, which seems unlikely. We expect many women to have been aware of a multiple pregnancy when reporting their TTP, although probably not when they accepted to participate in the study, but we do not believe this to have influenced their reporting. The overall frequency of twin deliveries in this population (including those resulting from infertility treatment) was 2.2%, fairly similar to the nationwide frequency of twins of 2% for the same years (Danish Association of Obstetrics and Gynecology).

It is possible that our failure to find an association between twinning and unplanned pregnancy resulted from the fact that women who had not planned a pregnancy and were pregnant with twins were less likely to continue the pregnancy, or less willing to join the cohort. However, we consider it very unlikely that women would have decided to interrupt their pregnancy (or to participate in the cohort) based upon the sex of the twins, and we therefore believe that our finding concerning the excess of same sex twins among women who conceived despite contraception is interesting and should be investigated further.

The observed relationship between TTP and twinning suggests that women who define themselves as pregnancy planners probably report their TTP accurately. It is possible nonetheless that reporting of infertility treatment is less reliable, at least for primiparas. The twinning rate among women reporting any kind of treatment, however, was 15.5%, whereas women with a TTP longer than 12 months and no report of treatment had a rate of twinning of 0.9%, suggesting that the degree of misclassification is small.

Our finding corroborates the notion that ‘natural’ twinning trends could be used as an indicator of reproductive health. Furthermore, if the link between fecundity and twinning is causal, then it is plausible that the long decline in twinning observed in the 1960s and 1970s could have been the result of a widespread decrease in fecundity simultaneously affecting many countries. The recent increase in twinning rates is probably due to infertility drugs, and we therefore do not know whether the ‘natural’ twinning rate in industrialized countries has been restored. Recent evidence suggests that young women in some countries may now have increasing twin rates (James, 1995; Astolfi et al., 2003), and we may never be able to discover what affected fecundity and if this mechanism is still acting.

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