Time to pregnancy and sex of offspring: cohort study

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The proportions of X and Y chromosome bearing sperms in human semen are equal, but more boys than girls are born. Male embryos and fetuses have a greater risk of attrition in utero than their female counterparts, and therefore male excess is likely to be still larger at the time of conception. It remains unexplained, however, what is responsible, presumably at some point between insemination and conception, for the greater probability of Y bearing sperms fusing with the ovum. One hypothesis relates to experiments showing that Y bearing sperms swim faster than X bearing sperms in viscous fluids.[1] For natural conception, human sperms have to penetrate cervical mucus, the viscosity of which varies among and within women.[2] Since mucal viscosity also influences the probability of conception,[2] we expected that natural conceptions that take longer to achieve are more likely to be male than quick conceptions. We tested our prediction by assessing the relation between time to pregnancy and sex of the offspring.

Participants, methods, and results

We analysed data of 5283 Dutch women who gave birth to singletons between July 2001 and July 2003. All of the women, at about 14 weeks of pregnancy, were recruited by midwives and gynaecologists (response rate 5283/7200, 73.4%). Mean age of the women at the time of conception was 30.5 years; 83% of their pregnancies were planned, and 47% were delivering their first baby.

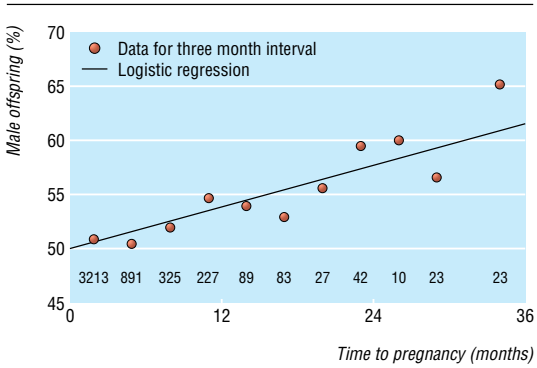
Among the 498 (9.4%) women with times to pregnancy longer than 12 months, the probability of male offspring was 57.6% (287), whereas the proportion of male births among the 4785 women with shorter times to pregnancy was 51.1% (2445, $\chi^2 = 7.81$, $P = 0.0052$). The proportion of male offspring after different times to pregnancy in the 4982 couples with natural conceptions is shown in the figure.

We modelled the relation between sex ratio (probability of male offspring divided by probability of female offspring) and time to pregnancy with logistic regression:

$\ln(\text{sex ratio}) = (0.0131 \times \text{time to pregnancy}) + 0.0116$ ($P = 0.0020$)

Using this function we computed that each additional year of trying to get pregnant is associated with a nearly 4% higher expected probability of delivering a male baby (see the line on the figure).

The association was robust to adjustment for maternal age, parity, body mass index, smoking status, alcohol use, season of conception, whether the pregnancy was planned or not, and variability of the menstrual cycle. Sex of the offspring of couples who had received medical help in getting pregnant (302) did not show any relation with time to pregnancy ($\beta = 0.0030$, $P = 0.59$).



Percentage male births for three month categories of time to pregnancy for 4982 Dutch women with natural conceptions. Numbers are births from which percentages were calculated; times to pregnancy of 31-36 months were combined for paucity of observations; percentage male births for times >36 months 71% (n=26)

Comment

The time taken to get pregnant is positively related to the chance of having a boy in couples conceiving naturally. The findings are consistent with the hypothesis that more viscous cervical mucus reduces the chance of conception and increases the chance of male offspring. Other explanations should nevertheless be considered. Firstly, while poor mucus quality may in itself be a cause of decreased fertility, it is often accompanied by hormonal problems and poor follicular development, conditions that may also give rise to lower birth rates by increasing the probability of early spontaneous abortion.[3] Secondly, after multiple unsuccessful attempts at getting pregnant, couples may increase their coital rate and optimise the timing of their coital acts. Higher coital rates might increase the odds of male offspring; better timing, however, seems to have the opposite effect.[4]

What is already known on this topic

The proportions of X and Y chromosome bearing sperms in human semen are equal, and male embryos and fetuses have a higher risk of dying in utero than their female counterparts. Nevertheless, throughout the world, more boys than girls are born

Y bearing sperm may be able to swim faster than X bearing sperm through relatively viscous cervical mucus

What this study adds

Taking longer to reach lasting pregnancy increases the chances of having male offspring, consistent with the hypothesis that poorly penetrable cervical mucus causes lower fecundity and higher likelihood of male offspring

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Previous work has considered a relation of offspring sex ratio with time to pregnancy.[5] A slightly reduced sex ratio was found in infertile couples (time to pregnancy >1 year). Comparison with the current findings, however, is complicated by the fact that no adjustments or subdivisions were made for assisted reproduction and the prevalence of reported infertility in the study population was unusually high (18%).

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Family history of breast cancer and cost of life assurance: a test case comparison of current UK industry practice

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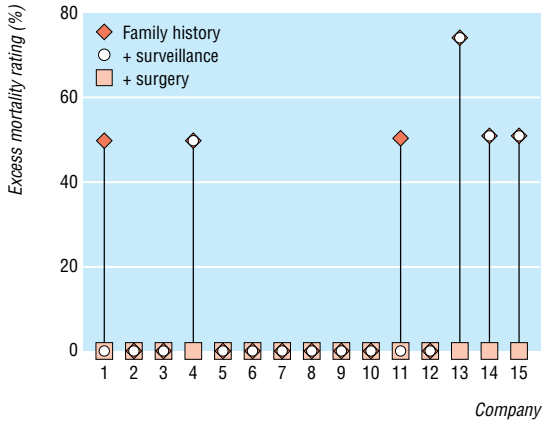
Under the current recently extended moratorium, applicants for life assurance need not disclose the results of predictive genetic tests.[1] The exception is for policies exceeding certain values, when insurers may seek results of tests approved by the government's Genetics and Insurance Committee. The committee expects to receive applications for the use of adverse results from tests for the BRCA1 and BRCA2 genes. Currently, insurers may, and often do, seek family histories. Substantial epidemiological data describe the relative risks of developing breast cancer depending on family history and age.[2] Preventive action for women at risk can include early enrolment on surveillance programmes and prophylactic surgery. Evidence is emerging for the benefits of the former,[3] and evidence is strong for risk reduction by the latter.[4 5]

Participants, methods, and results

We surveyed 21 companies representing 100% of the reinsurance market and 68% of the life and pensions market in the United Kingdom. We asked the companies to assess a fictional proposal for a 20 year policy (paying benefit only on death) by applying an excess mortality rating, defined as the percentage increase over the assumed rate of mortality. The applicant (scenario 1) was a 35 year old woman with unremarkable personal and family histories, except for breast cancer in the mother diagnosed at age 35. In line with standard insurance application forms, only first degree family history was given. In scenario 2, the same applicant had enrolled on a mammographic surveillance programme with no adverse results reported. In scenario 3, the same applicant had undergone prophylactic double mastectomy and oophorectomy (figure).

Sixteen companies responded. The responding and non-responding groups included a similar variety of company profiles (for example, global operations and size). Nine would not increase premiums under any of the scenarios. Six would increase premiums under scenario 1 (rating +50% or +75%), and of these, four would not load under scenario 3, and two would not load under either scenario 2 or 3. One small UK company would not raise premiums under scenario 1 or 2, but would apply an unspecified increase under scenario 3.



Percentage excess mortality ratings applied by life insurance and reinsurance companies in 2004-5. All companies gave one rating for the full product term, except for one that did not specify the rating or duration and is not shown

Comment

Most life insurance companies that responded to the survey would offer a standard premium in scenario 1 (unremarkable except breast cancer in the mother diagnosed at age 35). The lifetime relative risk of developing breast cancer for the applicant in scenario 1 is 5.7 (2.7 to 11.8).[2] Using life tables developed at the Cambridge Genetics Knowledge Park (A Butterworth, personal communication, 2005) this translates into a 20 year breast cancer mortality risk (from age 35) of 1.95%, compared with 0.6% for the general population—that is, three times higher.

It is reassuring that not only did all companies that rated under scenario 1 remove the rating after prophy-