A plea for data on the sexes of human offspring and the time of formation of the zygotes within the fruitful cycle

Sir,

Consider the proposition that the sex of a mammalian zygote is associated with the time of its formation within the mother’s cycle (herein Proposition 1). Hitherto, this has been regarded as, if true, a biological curiosity. However, it has been shown in a series of recent papers (James, 2008, 2009, in press) that if Proposition 1 were substantially true, then it could provide explanations for several well-established, but otherwise unexplained, phenomena including the following.

(i) The sex ratio (proportion male at birth) rose during and just after hostilities in most of the belligerent countries in World Wars 1 and 2, but not in subsequent or previous smaller engagements (James, 2009).

(ii) The regression of human sex ratio on duration of gestation is reverse-J-shaped. When very large quantities of data are examined, boys predominate at all reported gestations of 39 and fewer weeks, and at all reported gestations of >42 weeks. At reported gestations of 40–42 weeks, there are almost exactly equal numbers of boys and girls (James, 1994). The reason for this phenomenon is not established, despite its relevance to the initiation of labour. The argument, sometimes advanced by obstetricians, that fetal weight (or size) initiates labour, is apparently disproved by the excess of boys among births after 42 weeks gestation. Acceptance of a counter-argument (that the regression of sex ratio on gestation is caused by regression of sex ratio on time of formation within the cycle nine months earlier) is impeded by reluctance to accept Proposition 1 in the first place. Unfortunately, this remains the case, despite a meta-analysis of 10 independent studies, where the $P$-value of the resulting Mantel–Haenszel test statistic was 0.005 (James, 2000). To continue gathering evidence to elucidate this issue, I should like to appeal for more data relating offspring sex to the cycle day on which fruitful coitus occurred.

References


James WH. The variations of human sex ratio at birth with time of conception within the cycle, coital rate around the time of conception, duration of time taken to achieve conception and duration of gestation: a synthesis. J Theor Biol 2008;255:199–204.


ART register data on delivery rates

Sir,

We read with great interest the compendium of results of the assisted reproductive technology (ART) and intrauterine inseminations in Europe (Nyboe Andersen et al., 2009). We appreciate the difficulties associated with national data monitoring processes and with compilation and analysis of data from several countries which may have utilized different systems, standards and reporting methods. Despite all limitations and obstacles, the members of the European IVF Monitoring (EIM) Programme have managed to prepare a detailed report that gives an overview of the situation across the continent. The authors of the recent report, all whom have invested time and effort into this difficult task, should be commended.

We want to draw attention, however, to one fact which we found to be confusing during appraisal of the data with its current presentation format. The ultimate purpose of ART is the delivery of a healthy infant at term, and the delivery rate is the most relevant outcome parameter that reflects the effectiveness of our practice. We appreciate that a report not including delivery rates will be definitely incomplete and less useful to the reader. This notwithstanding, delivery rates in Italy, Spain, the Netherlands and Turkey as shown in Tables VI and VII seem to be unrealistic and confusing as presented in the manuscript. Although clinical pregnancy rates per cycle, per aspiration and per transfer for IVF cycles range between 19.2% and 26.4% for Italy, 29.2% and 35.8% for Spain, 19.4% and 24.5% for the Netherlands and 35.2% and 46.8% for Turkey, delivery rates per cycle, per aspiration, per transfer range between 8% and 11%, 9.9% and 12.1%, 9.6% and 12.8% for Italy, Spain and Turkey, respectively, and is reported to be 0% for the Netherlands (meaning that not even a single live birth has been reported for the year 2005). Similarly, the...
figures for clinical pregnancy rate after ICSI range between 18.6% and 23.9% for Italy, 31.5% and 36.2% for Spain and 34.7% and 37.2% for Turkey. Corresponding delivery rates are less than half of the reported clinical pregnancy rates (8.1–10.4%, 0%, 8.5–9.1% for Italy, the Netherlands and Turkey, respectively).

In our opinion, these differences are not biologically plausible, and merely reflect problems in data collection and reporting. One of the reasons for the presence of a large gap between pregnancy and delivery rates as reported by ART centres can be that the majority of women were followed and delivered in hospitals not connected with the ART centres that treated them. We think it would be prudent to omit delivery rates from the report whenever they are incomplete or unreliable. Besides being scientifically sound, this will also prevent unnecessary confusion about the actual delivery rates. Furthermore, access to the data presented by EIM by lay readers and infertile couples may lead to erroneous conclusions regarding success rates of individual clinics and countries.

Reference

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Reply: ART register data on delivery rates
Sir,
We would like to thank Dr Ata and Dr Urman for their interest in the reporting on delivery rates by the European IVF Monitoring (EIM) consortium of ESHRE (Nyboe Andersen et al., 2009).

The authors correctly point out that the delivery rates reported from a number of countries are unrealistically low. First of all, we are pleased that the authors appreciate the difficulties encountered in many clinics and registers regarding adequate follow-up of the outcome of pregnancies. Even though it may be difficult, we can only define the optimal end-point in ART, the birth rate, through complete and accurate reporting on deliveries. The concern is how to report in an appropriate way on birth rates in a world with incomplete follow-up on pregnancies. As this problem is likely to be consistent, at least for several years to come, it is appropriate to discuss how we should report on deliveries after ART.

The authors provide four examples. The extreme is the Netherlands, where no births were reported following treatment in 2005. The reason is that the National ART Register in the Netherlands has so far not included recording of any data on deliveries. We have not stated that it was 0, but we have simply left the spaces open in Tables VI and VII. Indeed, we could have made a footnote and stated this more explicitly, or indicated ‘NA’ for not available.

Regarding the data from the other three countries Italy, Spain and Turkey, it is also correct that the decline from the reported number of pregnancies to number of deliveries is huge. If we look at the ICSI data in Table VII, deliveries accounted for 43% (Italy), 44% (Spain) and 22% (Turkey) of the reported pregnancies. Evidently, this is underreporting of deliveries. The ideal would of course be to have complete recording of deliveries, or at least to have data on the number of pregnancies “lost for follow-up”. However, neither is recorded adequately in the registers at the present time.

In the EIM, we could provide estimations on the number of deliveries. From Table VII, we could select 12 countries (Belgium, Czeh Rep, Denmark, Finland, France, Germany, Norway, Portugal, Slovenia, Sweden, Switzerland and the UK) as a reference, because these ART registers have consistently reporting delivery rates for several years. These countries reported 26 980 ICSI pregnancies which resulted in 20 465 (76%) deliveries. It thus seems that around 76% of the pregnancies will result in birth, but the variability is not negligible, as it ranged from 64% in Germany to 89% in the UK. In Germany, the documented number of miscarriages does not cover the difference between pregnancy and delivery rates, as almost 1000 pregnancies are truly lost for follow-up. Therefore, the accurate figure on deliveries is undoubtedly higher. The calculations illustrate, however, that it will remain difficult to provide a reliable estimation of the true number of deliveries.

In both Tables VI and VII, a footnote is included stating that the recording of deliveries is incomplete. I presume that most professionals will realise this, but as Dr Ata and Urman stated, it is important because the data should be disclosed to the public, and misinterpretations may occur. We therefore agree with them that we should have addressed this issue more clearly.

In the EIM, we could simply have omitted all data on deliveries. We have discussed this option, but indeed both among professionals and patients, deliveries are the objective of ART and remain our gold standard in relation to defining efficacy. We therefore feel that the reporting of deliveries should be included—also in order to stress the importance of this key parameter.

A third possibility is to censor the reporting and only report on deliveries in those countries where we believe that the reporting is rather accurate. The problem here will of course be how to define the threshold for the lowest acceptable level of incompleteness of reporting. It could be easy if only one-third of all pregnancies resulted in a reported delivery, but what about for instance Russia where the number of deliveries reported was 59% of the recorded pregnancies in 2005. Should we then report deliveries from Russia or just delete the number available?

Our suggestion is that both National and Regional registers like the EIM continue to report on deliveries, but that we try to be more explicit in order to explain the inadequacy of the recording on deliveries. Finally, we would like to use this correspondence to stress the importance of establishing statutory registers, where recording of deliveries is compulsory and where data are validated.