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The male disadvantage and the seasonal rhythm of sex ratio at the time of conception

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BACKGROUND: In accordance with a presumed greater fragility of male versus female pregnancies, we tested whether sex ratio (male/female ratio) of vital pregnancies is higher in seasons more favourable for reproduction. METHODS: A retrospective study was performed on 14 310 births which had occurred in our institute between 1995–2001. For each single pregnancy the time of conception was calculated by the last menstrual period recall and confirmed or redefined by ultrasound in 95.8% of cases. The sex ratio of 199 454 pregnancies which had occurred in the Modena County between 1936–1998 was also stratified according to the month of birth. RESULTS: Sex ratio of institutional deliveries was 0.511 and was identical to that obtained from the County registry. Sex ratio at birth did not show a significant seasonal variation. By contrast, sex ratio calculated at time of conception showed a seasonal rhythm, with amplitude of 2.4% and peak values in October (confidence interval: ±43 days). The rhythm was in phase with the rhythm of conception that showed peak values in September (confidence interval: ±37 days) and an amplitude of 7%. CONCLUSIONS: The superimposition of the phase of sex ratio and conception rhythms supports the contention that more males than females are conceived in seasons with more favourable reproductive conditions.

Key words: conception/delivery/rhythms/seasons/sex ratio

Introduction

Determinants and determination of sex ratio have intrigued humans since antiquity. Indeed, the sex of a newborn has familial, social, cultural, medical and biological implications. Beside the fact that males are sometimes preferred, the bulk of evidence indicates that males are more fragile, and die earlier than females (Naeye *et al*., 1971; Calle *et al*., 1999). Fewer males are conceived in sub-optimal conditions than females. Sex ratio (male/female ratio) declines, as the consequence of environmental pollution (James, 1996a; Astolfi and Zonta, 1999; Mocarelli *et al*., 2000) destructive earthquakes (Fukuda *et al*., 1998), smoking parents (Fukuda *et al*., 2002), and aged mothers (Juntunen *et al*., 1997; Orvos *et al*., 2001) or fathers (Jacobsen *et al*., 1999; Nicolich *et al*., 2000). In particular the age of the parents becomes important in multiple pregnancies, when energy availability for the fetuses is more critical (Pollard, 1969; Juntunen *et al*., 1997; Jacobsen *et al*., 1999; Nicolich *et al*., 2000; Orvos *et al*., 2001). Endogenously generated anticipatory seasonal and diurnal rhythms are believed to favour adaptation to environmental changes and conservation of both the individual and the species. Seasons characterized by shortage of food and harsher environmental conditions are less favourable for litter survival. Accordingly, seasonal breeders synchronize their reproduction and consequently the time of delivery to seasons more favourable to newborn survival. Humans are not seasonal breeders, but human conception still follows a seasonal rhythm (Roennenberg and Aschoff, 1990; Cagnacci and Volpe, 1996), which probably allows young to be born in a more favourable environment. In accordance with this view, it is expected that fewer males are conceived in seasons less favourable to conception. A seasonal rhythm of sex ratio at time of birth was inconsistently reported, but when observed, its amplitude was small (about 0.5%) and its phase was not clearly related to the seasonal rhythm of conceptions (James, 1996b; Jongbloet *et al*., 1996; Lerchl, 1998). Sex ratio at birth may not reflect that at conception because the length of gestation may vary, and may be different between male and female fetuses (Cooperstock and Campbell, 1996; Bernstein, 1998; James, 2000). Accordingly, we evaluated the seasonal rhythm of sex ratio at time of conception and tested its phase relationship with that of reproduction.

Materials and methods

Data on 14 335 children born in the period 1995–2001 was obtained from the Institute of Obstetrics and Gynecology in Modena. Information on time of conception was present for 14 310 of the children. For each single pregnancy, time of conception had been obtained on the basis of last menstrual period recall and gynaecological examination. In 95.8% of the cases the calculated time of conception had been confirmed or redefined by an early pregnancy ultrasound examination. Modena is a small town with an estimated population of 49 984 women of fertile age (15–45 years), and our institute is the only point of reference in gynaecology and obstetrics. Accordingly, it is expected that almost all the normal and pathological pregnancies are referred to our institute, although it cannot be excluded that institutional hospitals of nearby smaller towns may admit several women from the Modena area and vice-versa. In order to evaluate whether institutional sex ratio reflected that of our area, we estimated the sex ratio of the pregnancies which had occurred in the Modena county between 1936–1998, from the County database.

For the institute database, sex ratio was stratified according to both the month of conception and the month of birth. The length of gestation of each single pregnancy, and the sex ratio of pregnancies terminated at different weeks of gestation was also calculated. For the County database, sex ratio was stratified according to the month of birth. Circa-annual rhythmic distribution of sex ratio and number of conceptions of vital pregnancies was evaluated by the periodogram method using the RHYTHM program (Van Cauter, 1979). The periodogram was adapted to analyse the 12 months rhythm. As originally described (Van Cauter, 1979), the method initially tests the significance of the observed time fluctuations against the hypothesis of their purely random occurrence via two different tests. The alternative to pure randomness is, for the first test, the existence of local correlations, implying that values at given times depend on values at other times, and for the second test, the existence of periodic fluctuations. When the hypothesis of random occurrence of the data is rejected, the periodogram method is applied to detect and estimate the possible significant components. A sum of sinusoidal components with periods equal to integer divisors of the observation span (i.e. 12 months/1; 12 months/2; 12 months/3; etc.) is fitted on the series. A decision procedure devised by Fisher (Van Cauter, 1979) allows the selection of the significant periodicity underlying the process at a given probability of $P < 0.05$. Up to the first three significant periodical components are included in the theoretical description of the profile. A theoretical pattern is computed according to the minimum of the residual sum of squares. The amplitude of the theoretical pattern is defined as half the difference between the maximum and minimum of the theoretical pattern, while the acrophase is the time corresponding to the occurrence of the first global maximum of the theoretical curve. Both the amplitude and the acrophase are furnished with a confidence interval. Periodograms are considered significantly different when described by different periodical components or alternatively when the confidence intervals of either the amplitude or acrophase do not overlap. Accordingly, the periodogram analysis estimations of the relative contributions of low and high components in the time dependence of the profile and indications regarding the frequency range and the periodicity or non-periodicity of any components are obtained. Contingency tables and the χ^2-test were used to perform the statistical comparison among sex ratio at different times of gestation and the sex ratio observed in the different seasons of the year.

Results

The sex ratio of deliveries within our institution was 0.511. An identical sex ratio was observed in the 199 454 pregnancies which had occurred in the Modena county between 1936–1998.

The analysis of the institutional medical records and the historical registry of the Modena county showed a slight circa-annual fluctuation of sex ratio evaluated at time of delivery. Fluctuations were similar for both analyses with peaks of sex ratio in March and September. In both analyses, these fluctuations were not significant at the periodogram evaluation.

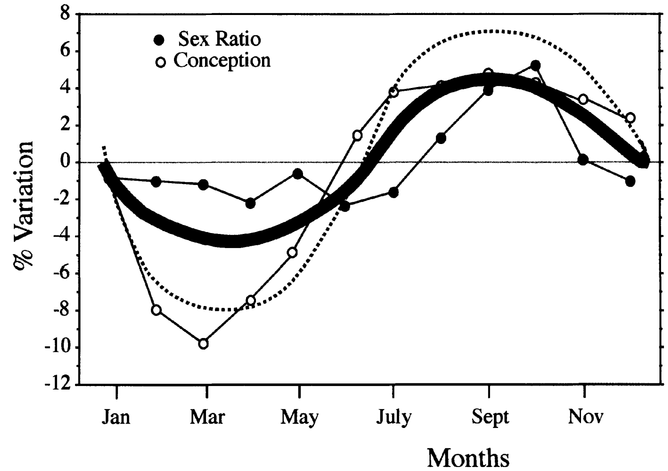

Figure 1. Seasonal variation of sex ratio and conception rate, evaluated at time of conception on 14 310 cases hospitalized between 1995–2001. Sinusoids represent the theoretical curves fitted to the actual data of rate of conception (dotted) and sex ratio (continuous).

From the institute's medical record we calculated that the sex ratio of fetuses born between 30–37 weeks (n = 2237) gestation was significantly higher than that observed in fetuses born between 40–42 weeks (n = 6013) gestation (0.525 versus 0.498; $P < 0.02$, χ^2). Intermediate sex ratio was observed in fetuses born between 38–39 weeks gestation (n = 5867; sex ratio = 0.519). Accordingly, at conception the rhythm of sex ratio was different from that at birth.

Indeed, sex ratio calculated at the time of conception showed a significant seasonal rhythm (period = 12 months) with an amplitude of 2.4% and a theoretical maximum in October (±43 days) (Figure 1). The sex ratio was significantly higher in the 3 months of the peak (September, October and November) than in the 3 months of nadir (March, April and May) (0.530 versus 0.504; $P < 0.05$).

The rhythm of sex ratio was in phase with that of conceptions calculated in the same set of data. Conception showed a seasonal rhythm with a period of 12 months, an amplitude of 7% and a theoretical maximum in September (±37 days) (Figure 1). The overlap between the confidence limits of the peaks indicates that the phase of the sex ratio rhythm is not significantly different from that of conception.

Discussion

A seasonal rhythm of human sex ratio has been inconsistently described (James, 1996a; Jongbloet *et al.*, 1996; Maconichie and Roman, 1997), and when observed its amplitude has been reported to be small (<0.5%) (James, 1996a; Jongbloet *et al.*, 1996; Lerchl, 1998). Indeed, also in our study, when sex ratio was calculated as in previous studies, at the time of birth, it showed a blunted seasonal variation, not significant at the periodogram analysis, with a major peak in March, and a minor one in September. Pregnancies terminating at different weeks of gestation show a different proportion of males in their offspring as previously (Cooperstock and Campbell, 1996;

Bernstein, 1998; James, 2000) and herein observed. Accordingly, the evaluation of sex ratio at birth may not reflect its seasonal rhythm at conception. The present study was designed to specifically test the seasonal rhythm of sex ratio at time of conception, defined as precisely as possible by the date reported in the medical records of each single pregnancy. Sometimes, the evaluation of the time of conception by anamnesis may be misleading (Gerrison, 1991) but in our study 95.8% of dates were validated or corrected by an early pregnancy ultrasound investigation. With this type of evaluation, the sex ratio defined at the time of conception showed a clear seasonal rhythm with amplitude higher than previously thought and a phase coincident with that of conception. Since sex ratio is more clearly identifiable at the time of conception, it is tempting to speculate that sex selection occurs in the early stage of pregnancy, probably already at the time of conception and/or embryo implantation (Mills and Robertshaw, 1981; Paraskevaides *et al*., 1988; Stolwijk *et al*., 1994; Ossenbhun *et al*., 1998). Indeed, several lines of evidence seem to indicate that production and implantation of male and female embryos shows a seasonal variation (Paraskevaides *et al*., 1988; Stolwijk *et al*., 1994; Ossenbhun *et al*., 1998). This may depend on the seasonal modifications of the endocrine environments of both parents (Ronkainen *et al*., 1985; Cagnacci and Volpe, 1996; Martikainen *et al*., 1996; Meriggiola *et al*., 1996; Ménézo *et al*., 1999), that ultimately influence semen quality (Levine *et al*., 1992) and oocyte (Jongbloet *et al*., 1996; Ménézo *et al*., 1999). An increased coital rate could bring an increase in secondary sex ratio (James, 1975; 1997), and whether present or not in seasons with high conception rate, may bring a synchrony between the rhythm of conception and that of the sex ratio. This possibility cannot be excluded although the seasonal rhythm of conceptions seems to be independent of coital rates, being also evident in IVF programmes, with a constant frequency in the procedures (Paraskevaides *et al*., 1988; Stolwijk *et al*., 1994; Ossenbhun *et al*., 1998). The data showing a prevalence of females in seasons with reduced fertility, and by contrast, an increased prevalence of males in seasons with increased fertility, support the hypothesis that a greater attrition on males is exerted in all those situations in which reproductive conditions are sub-optimal.

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