

Influences of maternal weight on the secondary sex ratio of human offspring

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BACKGROUND: Less than optimal reproductive conditions may be associated with a secondary sex ratio biased towards females. Body weight represents a critical determinant of reproduction. Accordingly, we evaluated whether preconception body weight and weight gain during pregnancy influence the sex ratio of human offspring. **METHODS:** A retrospective study was performed on 10 239 births in 1997–2001. Time of conception, preconception body weight and net weight gain during pregnancy were obtained for 9284 pregnancies. **RESULTS:** The secondary sex ratio of mothers in the lowest quartile of pre-pregnancy body weight (<54.6 kg) was lower than that of the other three quartiles (0.497 versus 0.525; $P < 0.01$). In contrast, the sex ratio of children born by the women in the highest quartile of weight gain during pregnancy appeared lower than that of the first three quartiles (0.493 versus 0.516; $P = 0.054$). **CONCLUSIONS:** A low pre-pregnancy weight and a greater weight gain during pregnancy are both associated with a reduced secondary sex ratio. These data indicate that in women with non-optimal reproductive/metabolic conditions, a greater attrition is exerted on male than on female offspring.

Key words: body weight/conception/metabolism/sex ratio

Introduction

Mechanisms defining the regulation of sex ratio in animals and humans have been debated for a long time. Several determinants, one of which is parents' conditions, seem to influence the sex ratio. In polygynous animals, parents in better condition would be expected to show a bias toward male offspring (Trivers and Willard, 1973). In humans, a sex ratio biased towards females has been observed in smoking parents (Fukuda *et al.*, 2002), in aged mothers (Juntunen *et al.*, 1997; Orvos *et al.*, 2001) in aged fathers (Jacobsen *et al.*, 1999; Nicolich *et al.*, 2000) and, by some authors, in women with metabolic alterations, such as diabetes (James, 1998; Rjasanowski *et al.*, 1998). One of the critical parameters for reproduction is the energy availability of the mother (Wade and Schneider, 1992). Because of this, it is possible that variation in maternal energy storage is associated with a modification of the secondary sex ratio. In this study, we evaluated whether maternal weight at conception or during pregnancy influences the sex ratio of human offspring.

Materials and methods

Data on 10 239 children born in the period 1997–2001 were obtained from the Institute of Obstetrics and Gynaecology in Modena, Italy. Information on time of conception, pre-pregnancy weight and weight gain during pregnancy was available for 9284 (90.6%) of the pregnancies. For each single pregnancy, time of conception had

been obtained on the basis of last menstrual period recall and gynaecological examination. In 95.1% of the cases the calculated time of conception had been confirmed or redefined by an early pregnancy ultrasound examination. Pre-pregnancy weight was registered on the basis of women's recall, while weight at time of delivery was measured for each woman. The institutional sex ratio was compared with that of the pregnancies, which had occurred in Modena County between 1936 and 1998, as obtained from the County database.

Pre-pregnancy weight, weight gain during pregnancy and weight at delivery were divided in quartiles, and sex ratio was stratified accordingly to the weight quartiles. In order to exclude the possibility that quartiles of weight gain during pregnancy are related to a different length of gestation or pre-pregnancy weight, length of gestation and pre-pregnancy weight was calculated for each quartile of weight gain during pregnancy. Contingency tables and the χ^2 -test were used to perform the statistical comparison between the different quartiles. A P -value of 0.05 was used to test the null hypothesis. The results are reported as mean $\pm$ SEM.

Results

The overall sex ratio was 0.515, which is slightly higher than the 0.511 observed in our County between 1936 and 1998.

Mean age $\pm$ SEM of the women was 31.12 ± 0.27 years, and did not stratify differently among the weight quartiles. Mean pre-pregnancy weight was 61.14 ± 0.05 kg, mean weight gain during pregnancy was 13.0 ± 0.02 kg and mean weight at time of delivery was 74.15 ± 0.05 kg. Weight limits defining

Table I. Weight values defining the four quartiles of pre-pregnancy weight, weight gain during pregnancy and weight at delivery

Quartiles	1st	2nd	3rd	4th
Pre-pregnancy weight (kg)	≤54	>54, ≤62	>62, ≤71	>71
Weight gain (kg)	≤10	>10, ≤13	>13, ≤15	>15
Weight at delivery (kg)	<67	>67, <72	>72, <79	>79

Table II. Sex ratio of deliveries stratified accordingly to the four quartiles of pre-pregnancy weight, weight gain during pregnancy and weight at delivery

Quartiles	1st	2nd	3rd	4th
Pre-pregnancy weight	0.497 ^a	0.536	0.519	0.519
Weight gain	0.511	0.511	0.533	0.493 ^b
Weight at delivery	0.499 ^c	0.542	0.476 ^d	0.523

^a $P < 0.003$ versus 2nd; $P < 0.01$ versus 2nd, 3rd and 4th considered as a whole.

^b $P < 0.02$ versus 3rd; $P = 0.054$ versus 1st, 2nd and 3rd considered as a whole.

^c $P < 0.003$ versus 2nd.

^d $P < 0.002$ versus 2nd and 4th.

the quartiles of pre-pregnancy weight, weight gain during pregnancy and weight at delivery are reported in Table I.

When stratified for the quartiles of pre-pregnancy weight, sex ratio was significantly lower in the 1st quartile than in the 2nd quartile ($P < 0.003$) (Table II). Intermediate values were observed in the 3rd and 4th quartiles (Table II). However, the sex ratio of women of the 1st quartile was significantly lower than that of women with a pre-pregnancy weight above this value (2nd, 3rd and 4th quartiles) (0.497 versus 0.525; $P < 0.01$).

Sex ratio stratified for weight gain showed similar values in the first three quartiles and lower values in the 4th quartile (Table II). The sex ratio of the 4th quartile was lower than that of the 3rd quartile ($P < 0.02$), and of the first three quartiles considered as a whole (0.493 versus 0.516; $P = 0.054$) (Table II). Mean length of gestation was 39.03 ± 0.02 days, and it did not stratify differently among the four quartiles of weight gain. Also, pre-pregnancy weight did not stratify differently among the four quartiles of weight gain.

Weight at delivery is the result of pre-pregnancy weight and weight gain during pregnancy. The sex ratio differed among quartiles of weight at delivery, with no clear trend (Table II).

Discussion

The present data indicate that maternal weight at conception influences the sex ratio of offspring. In particular, a low pre-pregnancy weight is associated with a deficit of males. The results are consistent with a recent reports showing that in rural Ethiopia, well-fed women were more likely to conceive males (Gibson and Mace, 2003), that the relationship between caloric availability and sex ratio is observed across several countries (Williams and Gloster, 1992), and that there is a higher energy demand for pregnancies with male embryos (Tamimi *et al.*, 2003). These data support the theory of Trivers and Willard

(1973), suggesting that a higher proportion of females are produced in non-optimal maternal conditions. The effect of pre-pregnancy weight on sex ratio can be exerted through a selection of gametes as well as through an increase in the rate of male embryo abortions.

Weight gain during pregnancy was also associated with modifications of secondary sex ratio. In particular, the greatest increase in weight was characterized by a decrease in the sex ratio. This was not observed in a recent study performed in a more limited number of pregnancies (Tamimi *et al.*, 2003). A greater increase in weight may be the consequence of an increased duration of gestation. Because pregnancies terminating at different weeks of gestation show a different proportion of male offspring (Cooperstock and Campbell, 1996; Bernstein 1998; James, 2000), a difference in length of gestation might explain the difference observed among the quartiles of weight gain. However, this possibility seems to be excluded by our analysis, which shows similar lengths of gestation in the four quartiles of weight gain. It is also possible that a greater increase in weight during pregnancy is the consequence of a low pre-pregnancy weight. Accordingly, women gaining more weight could be the same as the 1st quartile of pregnancy weight, i.e. those showing a reduced sex ratio in their offspring. This possibility also seems to be excluded by our analysis, which shows a similar pre-pregnancy weight among the four quartiles of weight gain. Weight gain during pregnancy may modify the secondary sex ratio only after conception and implantation, through an increase in the loss of male embryos. However, an alternative explanation is possible. The excessive increase of weight during pregnancy may indicate a metabolic tendency of the woman towards energy storage, rather than energy utilization, for reproductive processes. These mechanisms may be operative before pregnancy, and may influence sex ratio as early as at time of conception/implantation. Indeed, a reduction of sex ratio has been reported in women with diabetes (James, 1998; Rjasanowski *et al.*, 1998), probably as the consequence of an altered availability of essential fatty acids for the embryo (Crawford *et al.*, 1998).

Although the mechanisms underlying sex selection are still unclear, the data seem to indicate that males are more fragile (Naeye *et al.*, 1971), and that a greater attrition is exerted on them when reproductive/metabolic conditions are non-optimal (Crawford *et al.*, 1998). This view is supported by the documented decline of the sex ratio in the cases of unfavourable seasons (Cagnacci *et al.*, 2003), environmental pollution (James, 1996; 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).

The present study has several limitations. Most of the data were based on anamnesis, and errors could have been made in the exact recall of pre-pregnancy weight. The height of the

women was not recorded in the hospital charts, and it was not possible to calculate the body mass index, which would have allowed a better quantitation of fat stores. In addition, smoking habit data were missing from most of the records, and a different distribution of this parameter among the different quartiles cannot be excluded.

On the other hand, the data rather strongly indicate maternal weight, and probably maternal metabolism, as important determinants of secondary sex ratio in human offspring. The interaction of these parameters with other determinants of human sex ratio needs to be addressed in focused studies.

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