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Maternal Eating Disorders Influence Sex Ratio at Birth

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Abstract

We explored sex ratio at birth, defined as the proportion of male live births, in women with anorexia nervosa, bulimia nervosa, binge eating disorder, and eating disorders not otherwise specified-purging type (EDNOS-P) relative to a referent group in a large population based sample of 38,340 pregnant women in Norway. Poisson regressions were adjusted for mother's age, pre-pregnancy BMI, lifetime smoking status, maternal education, income, marital status, gestational age, and parity. Lower proportions of male live births were observed in the anorexia and bulimia groups, while binge eating disorder and EDNOS-P were associated with a higher proportion of male births. These data suggest that maternal eating disorders may influence offspring sex and that the direction of effect may vary by eating disorder subtype. If confirmed, this finding could provide evidence in formulating hypotheses regarding the consequences of eating disorders and determinants of sex ratio at birth.

Keywords

anorexia nervosa; bulimia nervosa; binge eating disorder; sex ratio at birth

Introduction

Sex ratio at birth, also known as the secondary sex ratio, has been shown to be influenced by factors that are known to be disturbed in women with eating disorders including maternal diet, stress, maternal pre-pregnancy weight, body fat distribution, and hormonal factors (1-5). Particularly noteworthy, low maternal weight, a diet low in certain fats, higher stress levels, and lower androgen levels have been associated with fewer male births (1-5). As part of a larger investigation of the impact of eating disorders on pregnancy outcome in a large population-based sample in Norway (6), we explored the impact of eating disorders on sex ratio at birth. To our knowledge, no reported association between maternal eating disorders and sex ratio at

birth exists. Given known relations among diet, stress, and anorexia nervosa, we hypothesized that there would be a lower proportion of male births in women with anorexia nervosa.

Material and Methods

The data collection was conducted as part of the Norwegian Mother and Child Cohort Study (MoBa) at the Norwegian Institute of Public Health (7). The study has been approved by the Institutional Review Board of the University of North Carolina at Chapel Hill and appropriate regional committees for ethics in medical research and the Norwegian National Data Inspectorate.

MoBa is a prospective pregnancy cohort study. Pregnant women are recruited through a postal invitation after registering for a routine prenatal ultrasound at about 18 weeks' gestation. Participating women sign informed consent, donate blood and urine samples, and receive a questionnaire. The present study is based on the first questionnaire. The MoBa cohort is linked to Norwegian health registries, particularly the Medical Birth Registry of Norway (8) to capture pregnancy outcome variables.

Questionnaire 1 included items on eating disorders and behaviors derived from studies of the Norwegian Institute of Public Health Twin Panel (9) that reflected DSM-IV criteria for eating disorders (10). Diagnostic algorithms captured: broadly defined anorexia nervosa (DSM IV criteria excluding amenorrhea and endorsing a body mass index (BMI) $<18.5 \text{ kg/m}^2$ at the time of low weight); broadly defined bulimia nervosa (DSM IV criteria endorsing at least weekly frequency of binge eating and purging and categorized as any type, purging type, non-purging type); broadly defined binge eating disorder (DSM IV criteria with at least weekly frequency of binge eating in the absence of compensatory behaviors), and eating disorders not otherwise specified-purging type (EDNOS-P; purging at least weekly in the absence of binge eating). Anorexia nervosa was assessed before pregnancy only due to the practical difficulties in determining low weight in the presence of pregnancy-related weight gain. Bulimia nervosa, binge eating disorder, and EDNOS-P were assessed for both 6 months prior to pregnancy (retrospective assessment) and at the time of survey completion. Respondents were asked to distinguish between pregnancy-related nausea and vomiting and self-induced vomiting as a purging method. Self-reported weight and height were used to calculate BMI measures. A total of 38,340 respondents completed questionnaire 1 at a median of 18.6 weeks gestation (inter-quartile range 17.1-20.4 weeks and range 6.0-42.3 weeks).

The sex ratio at birth (the proportion of male live births) estimates were based on all women with singleton live births and eating disorder diagnoses. Poisson regression was used to estimate unadjusted and adjusted proportions and ratios with generalized estimating equations to estimate variance for this sample as described by Bulik et al. (6). Analyses were adjusted for factors known to affect sex ratio at birth including mother's age, pre-pregnancy BMI, lifetime smoking status, maternal education, combined income index, marital status, gestational age, and parity. All analyses were performed using SAS/STAT software for Windows and AIX, version 9.1 (11).

Results

Sex ratio at birth estimates are presented in Table 1. Unadjusted estimates showed 10% and 9% lower proportions of male live births for mothers with anorexia nervosa and bulimia nervosa, respectively, whereas maternal binge eating disorder and EDNOS-P were associated with 4% and 28% higher proportion of male births relative to the referent. After adjusting for relevant covariates, the risk ratio effects changed less than 2% in value for all eating disorder subtypes.

Discussion

These findings suggest an association between eating disorders and sex ratio at birth in the hypothesized direction for anorexia nervosa and bulimia nervosa and in the opposite direction for binge eating disorder and EDNOS-P. The sex ratio at birth for the non-eating disorder population in these estimates, 1.04, closely matches previous Norwegian estimates of 1.05 (12) and 1.06 (13).

Hormonal and body composition changes, which are reported to affect sex ratio at birth as noted above, occur with both gestational age and parity. Moreover, parity (14) and age (15) may themselves affect the sex ratio at birth. However, controlling for several critical factors did not alter the estimates indicating a robustness of the eating disorder subtype association with sex ratio at birth. Despite the large sample, the small numbers of participants reporting anorexia nervosa and EDNOS-P contribute to large variability in their estimated sex ratios at birth. Replication of analyses using birth registries and retrospective histories are required to corroborate the observed association.

Nonetheless, these data suggest that maternal eating disorders may influence offspring sex and that the direction of effect may differ depending on eating disorder subtype. Whether this effect stems from maternal diet, stress, hormonal levels or other factors affiliated with both eating disorders and sex ratio remains unknown. Furthermore, the sex ratio differences across subtypes can exist at the primary sex ratio level. It is also unknown whether the effects of a maternal eating disorder on sex ratio operate periconceptually, for example by preferential fertilization of the oocyte by x- or y- bearing sperm (5,16), or post-conceptionally, in anorexia and bulimia nervosa, with an increased loss of male fetuses because of an increased susceptibility to poor nutrition or intrauterine stressors (17). If confirmed, this finding could provide evidence in formulating other hypotheses regarding the consequences of eating disorders and possible determinants of sex ratio at birth.

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Table 1

Sex-ratio at birth estimates across eating disorder subtypes.

Eating Disorder	Sex ratio at birth	Proportion Male		Risk Ratio (95% CI)	
		Male births/total births	Unadjusted (95% CI)	Unadjusted	Adjusted*
Anorexia nervosa	0.84	16 / 35	0.46 (0.32, 0.66)	0.90 (0.63, 1.29)	0.89 (0.62, 1.27)
Bulimia nervosa	0.89	157 / 334	0.47 (0.42, 0.53)	0.92 (0.82, 1.04)	0.93 (0.83, 1.04)
EDNOS-P	1.86	26 / 40	0.65 (0.52, 0.82)	1.28 (1.02, 1.60)	1.28 (1.02, 1.60)
Binge eating disorder	1.12	1044 / 1978	0.53 (0.51, 0.55)	1.04 (0.99, 1.08)	1.04 (0.99, 1.08)
No eating disorder	1.04	18288 / 35953	0.51 (0.50, 0.51)		

* adjusted for mother's age, pre-pregnancy BMI, lifetime smoking status, maternal education, combined income index, gestational age, and parity.

Abbreviation: EDNOS-P: eating disorder not otherwise specified purging type