

Subfecundity in overweight and obese couples

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BACKGROUND: Recent studies indicate that not only women's but also men's obesity has adverse effects on fecundity and since fecundity is a couple concept, we examined fecundity in relation to overweight and obesity of the couple. We also examined the association between weight changes and fecundity over time. **METHODS:** Between 1996 and 2002, 64 167 pregnant women enrolled in the Danish National Birth Cohort were interviewed during and 18 months after pregnancy. Information on body mass index (BMI) and waiting time to pregnancy (TTP) was available for 47 835 couples. **RESULTS:** Among men and women with a BMI of 18.5 kg/m² or more, we found a dose-response relationship between increasing BMI group and subfecundity (a TTP of more than 12 months): Odds ratio (OR) = 1.32 (95% CI: 1.26–1.37) for women and OR = 1.19 (95% CI: 1.14–1.24) for men. Among 2374 women with an initial BMI of 18.5 kg/m² or more, who participated more than once in the Danish National Birth Cohort, each kilogram increment in weight between the two pregnancies was associated with a 2.84 (95% CI: 1.33–4.35) days longer TTP. **CONCLUSIONS:** Couples have a high risk of being subfecund if they are both obese.

Keywords: fecundity/fertility/obesity/overweight

Introduction

The 'obesity epidemic' seen in many countries is a serious threat to public health and a reduced capacity to reproduce is a potential but less well-known health hazard related to obesity.

Women's overweight is a risk factor for reduced fecundity (Bolumar *et al.*, 2000; Diamanti-Kandarakis and Bergiele, 2001), and recently men's obesity has also been linked with subfecundity (Sallmen *et al.*, 2006), as well as reduced semen quality (Jensen *et al.*, 2004). Since overweight and obesity tend to cluster in couples, it is important to have risk estimates for couples rather than individuals. We examined the association between different combinations of men's and women's body mass index (BMI) on fecundity in couples enrolled in the large Danish National Birth Cohort. For women having more than one birth, we also studied whether a change in weight between the two births correlated with a change in waiting time to pregnancy (TTP).

Materials and methods

The Danish National Birth Cohort is a nationwide study of pregnant women and their offspring (Olsen *et al.*, 2001). Between 1996 and 2002, more than 100 000 pregnant women were enrolled in the

cohort and interviewed by telephone twice during pregnancy (around 16th and 30th weeks of gestation) and twice after birth (around six and 18 months post-partum), however not all women completed all four interviews. Information on TTP, women's weight and height, previous pregnancies, men's and women's smoking habits and socioeconomic group of both men and women was obtained in the first interview, which was completed by 92 892 women. Information on the men's weight and height was obtained in the fourth interview, in which 66 712 women participated. In total, 64 167 women completed both the first and the fourth interview. The study was approved by the Institutional Review Board at University of California, Los Angeles (UCLA) and the Danish Data Protection Agency.

Of the 64 167 women who completed both interviews, we initially included couples that provided information on TTP ($n = 57\,103$) because they had planned or partly planned their pregnancies, and for whom we had data on BMI for both the man and the woman ($n = 60\,228$). This resulted in a total of 53 910 couples. We then excluded couples if the woman reported diseases that could impact her BMI and/or fecundity: metabolic or eating disorders ($n = 1117$ and 2170, respectively), cancers ($n = 81$), chlamydia ($n = 2236$), closed or removed Fallopian tube(s) ($n = 158$), malformed uterus ($n = 9$), endometriosis ($n = 194$), vulvodynia ($n = 3$) and positive for HIV ($n = 1$). Couples who used donor sperm to achieve the pregnancy were also excluded ($n = 106$) and thus 47 835 couples remained available for the analyses. Of the 47 835 couples, 2478 had at least two

births, where the same man was reported to be the father of both children. These were used for the analyses of the possible impact of weight change between the two pregnancies on TTP.

According to the criteria used by the World Health Organization (2000), we classified men and women as underweight (BMI < 18.50 kg/m²), normal weight (BMI: 18.50–24.99 kg/m²), overweight (BMI: 25.00–29.99 kg/m²) or obese (BMI ≥ 30.00 kg/m²). Subsequently, each couple was categorized into one of the 16 different possible combinations of man/woman BMI groups (normal/normal, normal/overweight, underweight/obese, etc.). Subfecundity was defined as a waiting time of more than 12 months (or 6 months) to achieve a pregnancy that resulted in a live birth.

Statistical analysis

We used multiple logistic regression models to calculate the confounder-adjusted odds ratios (ORs) for subfecundity according to BMI combination, using the different BMI combinations as a categorical explanatory variable and normal weight as reference. When testing for trend, the BMI groups were entered in the model as a continuous variable.

For confounder-adjustment, we included in the final model a combination of pre-selected covariates (men's and women's age) and covariates that changed the estimates of interest more than 10% when they were removed from the full model (Maldonado and Greenland, 1993). The latter group of covariates comprised previous pregnancies, combined socio-economic group and men's and women's smoking habits. The final selection of covariates is given in the footnotes of Table 1.

Using a multiple linear regression model, we evaluated the association between women's weight gain or loss and TTP among couples who participated more than once in the Danish National Birth Cohort. We adjusted for the partner's change in weight, changes in smoking habits and the length of the inter-birth interval.

Analyses were performed with 'Stata 8.2' (Stata Corporation, USA). All ORs are given with 95% confidence intervals (CIs).

Results

In this cohort, we had 6.8% obese men, 8.2% obese women and 1.4% couples where both were obese. The percentages of

persons with normal weight were 53% for men and 68% for women. The study group is further characterized in Table 2.

Among those with a BMI of 18.5 kg/m² or more, we found a dose-response relationship between BMI and OR for subfecundity among both men and women in different BMI combinations (Table 1). Crude estimates (not shown) were close to the adjusted estimates. We evaluated the OR for subfecundity according to BMI for both sexes separately, but adjusted for the partners BMI group, and found a slightly higher OR trend for women than for men (average increase in OR by increment in BMI group of 1.32 for women and 1.19 for men).

Among couples, where both were either overweight or obese, the adjusted ORs for subfecundity were 1.41 (95% CI: 1.28–1.56) and 2.74 (95% CI: 2.27–3.30), respectively, compared with couples, where both had normal weight.

Repeating the analysis using a 6 months TTP as cut-off level gave results similar to those reported. Restricting the analysis to only first pregnancies in the Danish National Birth Cohort ($n = 45\,343$) produced similar results as well.

We evaluated the association between women's weight gain or loss and TTP among 2374 couples who participated more than once in the Danish National Birth Cohort and where the woman's initial BMI was 18.5 kg/m² or more. We adjusted for the partner's change in weight, changes in smoking habits and length of the inter-birth interval. Each 1-kg increment in weight was associated with 2.84 (95% CI: 1.33–4.35) days longer TTP. Among 365 women, who had a BMI of 25.00 kg/m² or more before the first pregnancy and either lost weight or maintained the same weight (± 1 kg) in the time up to the next pregnancy, each 1 kg decrement in weight was associated with 5.50 (95% CI: 1.35–9.65) days shorter TTP. For women who started out with a BMI of less than 18.5 kg/m² ($n = 89$), we saw a tendency for a decreasing TTP for the second pregnancy when compared with the first with increased weight [regression coefficient: -3.82 (95% CI: -20.00 to 12.36) days/kg].

Discussion

We found higher risk of subfecundity related to overweight and obesity for both men and women, particularly for couples where both were overweight. Underweight combined with obese

Table 1. Odds ratios (ORs) for subfecundity (time to pregnancy of > 12 months) according to categories of men's and women's BMI

| Women's BMI (kg/m ²) | Men's BMI (kg/m ²) | | | | Women ^a OR (95% CI) |
|-------------------------------------|--------------------------------|----------------------------|----------------------------|--------------------|-----------------------------------|
| | <18.50 OR (95% CI) | 18.50–24.99 OR (95% CI) | 25.00–29.99 OR (95% CI) | ≥30 OR (95% CI) | |
| <18.50 | N/A | 1.00 (0.82–1.22) | 1.20 (0.94–1.53) | 1.95 (1.06–3.58) | 1.02 (0.88 to 1.18) |
| 18.50–24.99 | 0.69 (0.34–1.38) | 1.00 (Reference group) | 1.18 (1.10–1.27) | 1.53 (1.32–1.77) | 1.00 |
| 25.00–29.99 | 1.63 (0.67–4.01) | 1.36 (1.23–1.50) | 1.41 (1.28–1.56) | 1.79 (1.49–2.14) | 1.27 (1.18–1.36) |
| ≥30 | 3.79 (1.48–9.74) | 1.74 (1.51–2.02) | 2.07 (1.82–2.36) | 2.74 (2.27–3.30) | 1.78 (1.63–1.95) |
| Men ^b | 0.97 (0.61–1.54) | 1.00 | 1.15 (1.09–1.22) | 1.49 (1.34–1.64) | — |

N/A, too few observations.

All OR's are adjusted for men's and women's age, number of previous pregnancies, and socio-economic group. For the marginal values, we also adjusted for partners BMI.

^aOR for trend_(normal weight, overweight, obese) = 1.32 (1.26–1.37), $P < 0.001$.

^bOR for trend_(normal weight, overweight, obese) = 1.19 (1.14–1.24), $P < 0.001$.

Table 2. Characteristics of couples stratified by combinations of men's and women's BMI

| BMI combinations ^a | | <i>n</i> (%) (<i>n</i> 47 835 = 100%) | Subfecund (TTP > 12 months) <i>n</i> (%) | Prima gravida <i>n</i> (%) | Socioeconomic group I ^b <i>n</i> (%) |
|-------------------------------|---------------|---|--|-------------------------------|--|
| Men | Women | | | | |
| Underweight | Underweight | 10 (0.02) | 0 | 6 (60.00) | 5 (50.00) |
| Normal weight | Underweight | 1176 (2.46) | 128 (10.88) | 404 (34.35) | 826 (70.24) |
| Overweight | Underweight | 652 (1.36) | 84 (12.88) | 198 (30.37) | 428 (65.64) |
| Obese | Underweight | 75 (0.16) | 14 (18.67) | 18 (24.00) | 39 (52.00) |
| Underweight | Normal weight | 122 (0.26) | 9 (7.38) | 49 (40.16) | 79 (64.75) |
| Normal weight | Normal weight | 18 445 (38.56) | 2130 (11.55) | 6733 (36.50) | 13 859 (75.14) |
| Overweight | Normal weight | 12 235 (25.58) | 1665 (13.61) | 4236 (34.62) | 8681 (70.95) |
| Obese | Normal weight | 1579 (3.30) | 266 (16.85) | 537 (34.01) | 972 (61.56) |
| Underweight | Overweight | 38 (0.08) | 6 (15.79) | 12 (31.58) | 20 (52.63) |
| Normal weight | Overweight | 4422 (9.24) | 640 (14.47) | 1437 (32.50) | 2899 (65.56) |
| Overweight | Overweight | 4230 (8.84) | 665 (15.72) | 1391 (32.88) | 2601 (61.49) |
| Obese | Overweight | 908 (1.90) | 176 (19.38) | 325 (35.79) | 452 (49.78) |
| Underweight | Obese | 22 (0.05) | 7 (31.82) | 12 (54.55) | 11 (50.00) |
| Normal weight | Obese | 1500 (3.14) | 269 (17.93) | 508 (33.87) | 796 (53.07) |
| Overweight | Obese | 1747 (3.65) | 363 (20.78) | 548 (31.37) | 894 (51.17) |
| Obese | Obese | 674 (1.41) | 177 (26.26) | 232 (34.42) | 325 (48.22) |

^aUnderweight: BMI < 18.50 kg/m²; normal weight: BMI 18.50–24.99 kg/m²; overweight: BMI 25.00–29.99 kg/m²; obese: BMI ≥ 30.00 kg/m².

^bSocioeconomic group I corresponds to white collar workers and people currently receiving academic training.

partners, especially underweight men, seemed to cause additional pregnancy delays. The TTP increased with increasing weight gain between two births for women with an initial BMI of 18.5 kg/m² or more, which indicates a causal association between BMI, or correlates of BMI and fecundity.

Our results (ORs) for men are in accordance with those found by Sallmén *et al.* (2006), although their study population was much smaller (*n* = 2111 couples) and also included couples who had unsuccessfully tried to conceive. Men's BMI is reported to be associated with semen quality and/or the level of reproductive hormones (Jensen *et al.*, 2004; Magnusdottir *et al.*, 2005; Fejes *et al.*, 2006; Kort *et al.*, 2006), and semen quality and fecundity are correlated (Bonde *et al.*, 1998; Zinaman *et al.*, 2000), albeit not with strong coefficients (Slama *et al.*, 2004). In women, obesity has negative impact on ovulation, conception, implantation and early fetal development may also be adversely affected (Gosman *et al.*, 2006). In addition, obese women frequently suffer from polycystic ovary syndrome (Barber *et al.*, 2006). Since reliable data on frequency and timing of sexual intercourse were not available, we cannot exclude that infrequent intercourse (Brody, 2004) has delayed conception in overweight and obese couples.

Information on the men's height and weight were obtained in the interview approximately 18 months post-partum and thus more than 2 years after the conception, and even longer after the time of interest (start of TTP). For both the men and women there may be a differential (i.e. related to waiting TTP) misclassification of their weight. A longer TTP could both be associated with an increase (stress-induced eating) or a decrease in weight (advice to lose weight). The direction of this possible reverse causation could therefore be in both directions. We did not report changes in TTP followed by men's weight changes between two births because the timing of their weight data may be too imprecise for short inter-birth intervals. For the 586 couples with an inter-birth interval above 149 weeks

(the 75th percentile), we did, however, estimate the association and found a result close to that reported for women [regression coefficient: 2.48 (95% CI: −0.49 to 5.46) days/kg].

Since we know nothing of the reasons for changing weight between two pregnancies, analysis of weight change and TTP should be read with caution, especially for those who lose weight, since the results could be confounded by diseases related to weight loss.

Strengths of our study include a large sample size and use of data collected shortly after conception, where recall of TTP should be good. BMI data were based on self-reports, which poses a risk of underestimating BMI's (Jalkanen *et al.*, 1987), but this underestimation is probably not related to TTP. Couples with missing BMI information for the man, the woman or for both were not included in the study. We did, however, repeat the main analysis on OR for subfecundity according to BMI for each sex (adjusting for partners BMI), including couples with missing BMI data. This analysis included 49 957 couples, and we found results close to those presented in the Table 1, which suggests no selection bias caused by excluding those with missing data. The OR for subfecundity in women with missing BMI (*n* = 781) was, however, 1.45 (95% CI: 1.19–1.76) when compared with normal weight women. This higher risk of subfecundity indicates that overweight women were over-represented among the non-responders. For men, no such excess risk was found. Among those without a recorded TTP and therefore excluded from the study, the BMI distribution was similar to what we report for the participants.

Since our study only included couples who became pregnant, an association between a high BMI and sterility is not detectable. We believe, however, that the effect of BMI is quantitative rather than qualitative, if it is a cause of subfecundity, and this is supported by all existing studies. A high

BMI leads probably only to sterility in persons with additional fecundity problems.

We excluded couples if the women reported diseases that could impact her BMI and/or fecundity, but we cannot conclude that body fat causes the associations we saw. There may be an underlying cause of both overweight and reduced fecundity.

We found 2.3 times more couples where both were obese than could be expected for independent events, and assortative mating could contribute to a population increase in obesity genes (Hebebrand *et al.* 2000). Our results suggest that such an effect may be counteracted by a lower fecundity in obese couples, at least in populations with large fertility.

Overweight and obese couples have a higher risk of being subfecund. Whether losing weight brings fecundity back to normal values is best studied in a randomized trial among overweight couples who want to have a child in a near future. Our study indicates that it may be the case.

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