Obesity and pregnancy: complications and cost\textsuperscript{1–3}

Florence Galtier-Dereure, Catherine Boegner, and Jacques Bringer

ABSTRACT The prevalence of obesity is currently rising in developed countries, making pregravid overweight one of the most common high-risk obstetric situations. Although the designs and populations of published studies vary widely, most authors agree that pregravid overweight increases maternal and fetal morbidity. Even moderate overweight is a risk factor for gestational diabetes and hypertensive disorders of pregnancy, and the risk is higher in subjects with overt obesity. Compared with normal weight, maternal overweight is related to a higher risk of cesarean deliveries and a higher incidence of anesthetic and postoperative complications in these deliveries. Low Apgar scores, macrosomia, and neural tube defects are more frequent in infants of obese mothers than in infants of normal-weight mothers. The regional distribution of fat modulates the effects of weight on carbohydrate tolerance, hemodynamic adaptation, and fetal size. Maternal obesity increases perinatal mortality. Long-term complications include worsening of maternal obesity and development of obesity in the infant. The average cost of hospital prenatal and postnatal care is higher for overweight mothers than for normal-weight mothers, and infants of overweight mothers require admission to neonatal intensive care units more often than do infants of normal-weight mothers. Preconception counseling, careful prenatal management, tight monitoring of weight gain, and long-term follow-up could minimize the social and economic consequences of pregnancies in overweight women. Am J Clin Nutr 2000;71(suppl):1242S–8S.

KEY WORDS Obesity, waist-to-hip ratio, pregnancy, gestational diabetes, hypertension, macrosomia, mortality, cost

FREQUENCY OF OVERWEIGHT AMONG PREGNANT WOMEN

As the prevalence of obesity has risen in developed countries, overweight among pregnant women has become increasingly common. In the United States, the incidence of obesity among pregnant women ranges from 18.5% to 38.3%, according to the cohort studied and the cutoff point used to define overweight (1–6). Pregravid overweight is therefore one of the most frequent high-risk obstetric situations.

To determine the frequency of obesity during pregnancy in a region where the incidence of obesity in the general population is low, we undertook a study in Montpellier, France. Our series included 435 pregnant women seen consecutively at the Obstetric and Gynecology Department of Montpellier University Hospital during the third trimester of their pregnancy. The women were recruited between October 1993 and December 1994 and gave their informed consent to participate in the study. Seventy-four women (17.0%) had a body mass index (BMI; in kg/m\textsuperscript{2}) > 25 and 54 women (12.6%) had a BMI > 26 before becoming pregnant (Table 1). Also shown in Table 1 is the frequency of obesity among pregnant women or women of childbearing age in different cohorts in which relative weight before pregnancy was reported (1–8).

OUTCOME OF PREGNANCY IN OVERWEIGHT WOMEN: DIFFERENCES IN STUDY DESIGNS

Pregnancy outcome in overweight mothers was addressed as early as 1945 (9). Since then, study designs have varied widely (1, 3, 10–20). Differences in types of studies, thresholds used to define overweight, and definitions of control patients can result in major discrepancies in the data provided. Shown in Table 2 are some differences in definitions of overweight and choices of control groups in studies addressing the outcome of pregnancy in overweight women published since 1945. Other important differences include the time and length of the study period, the choice of exclusion criteria (eg, previous maternal pathology, multiple pregnancies, and stillbirths), and the characteristics of the population studied (eg, age, ethnic origin, and social background). Therefore, although most authors agree that pregravid overweight increases maternal and fetal morbidity, detailed comparisons between reports may be hazardous, and for some complications, rates vary within a broad range.

MATERNAL MORBIDITY

Carbohydrate intolerance

Overweight is a risk factor for impairment of carbohydrate tolerance both in the nonpregnant state and during pregnancy. Fasting postabsorptive plasma insulin concentrations are higher in obese pregnant women than in nonobese pregnant women (21). However, insulin secretion is increased enough in many obese women to maintain normoglycemia. Conversely, approximately

\textsuperscript{1}From the Service d’Endocrinologie and the Service de Maladies Métaboliques, Hôpital Lapeyronie, CHU Montpellier, France.


\textsuperscript{3}Address reprint requests to F Galtier-Dereure, Service d’Endocrinologie, Hôpital Lapeyronie, 371 Avenue du Doyen Gaston Giraud, F-34295 Montpellier Cedex 5, France. E-mail: ofdereure@wanadoo.fr.
half of women diagnosed with gestational diabetes have no identifiable risk factor (22). Therefore, other factors must be sought to explain the occurrence of gestational diabetes.

The regional distribution of fat was suggested to modulate the response to an oral glucose load in obese women (23). In this study, insulin areas under the curve after an oral glucose tolerance test (OGTT) during the second and third trimester of pregnancy and in the postpartum period were significantly higher in pregnant women with upper-body obesity than in pregnant women with lower-body obesity and in lean pregnant women. The same study reported a positive correlation between waist-to-hip ratio and glucose concentration and insulin areas under the curve.

No epidemiologic investigation of the importance of regional distribution of fat as a risk factor for gestational diabetes has been undertaken so far, but weight excess clearly increases the risk of overt impairment of carbohydrate tolerance in pregnant women. Even in moderately overweight subjects (BMI 25–30 or weight 120–150% of ideal body weight), the incidence of gestational diabetes is 1.8 to 6.5 times greater than that in normal-weight subjects (1, 3, 14, 16). In obese women, BMI > 30 or weight > 150% of ideal body weight, the incidence of gestational diabetes is 1.4- to 20-fold higher than that in normal-weight subjects (1, 3, 10–14, 16–20).

Screening for gestational diabetes must be performed early to allow for efficient management. In obese women, however, a negative test result at the 24th-week screening does not rule out the possibility that diabetes mellitus will develop later. Therefore, we suggest performing repeated acceptable screening tests (such as measuring fasting and postprandial glycemia) throughout pregnancy in this high-risk group, rather than performing a single OGTT between the 24th and 28th week of gestation.

If carbohydrate intolerance is diagnosed, tight metabolic control should be achieved through diet and, when indicated, insulin therapy. The American Diabetes Association recommends an average daily intake of 100 kJ/kg for obese mothers with gestational diabetes (24). Greater energy restrictions have been proposed (25), but with the risk of excessive ketogenesis. Whether ketone bodies impair fetal development and long-term child outcome is still unclear. Thus, if control of glycemia is poor with standard diet alone, insulin therapy should be initiated. Insulin treatment of gestational diabetes is required more often in obese women than in lean women (26) and reduces maternal and fetal morbidity (27, 28). In obese mothers with gestational diabetes, insulin treatment increases neither maternal weight gain during pregnancy (27) nor long-term adiposity in the offspring (29).

### Hypertensive disorders

Maternal hemodynamic changes in obese mothers include higher arterial blood pressure, hemoconcentration, and altered cardiac function (30). Hypertensive disorders are significantly more prevalent in obese pregnant women than in their lean counterparts. Even when overweight is moderate, the occurrence of hypertension and preeclampsia is significantly higher by comparison with control patients (1, 3, 14, 16). In obese women, the incidence of hypertension is 2.2–21.4 times higher than in control subjects, and preeclampsia occurs 1.22–9.7 times more often (1, 3, 10–14, 18, 19). In a case-control study of 66 women with eclampsia who were matched with 264 control subjects, a tendency toward an increased risk of eclampsia in the obese women, although not statistically significant, was reported (odds ratio: 2.49; 95% CI: 0.78, 7.96) (31). Although hypertension in obese women is associated with a reduction in subcutaneous fat of the newborn (32), the incidence of small-for-gestational-age infants is usually not higher in obese patients than in normal-weight control subjects.

In nonpregnant subjects, hypertension is associated with upper-body rather than with lower-body obesity. Similarly, the regional distribution of fat may modulate the risk of cardiovascular disease in pregnant women. In a study involving 22 patients with preeclampsia and 126 control subjects, the ratio of upper-body to lower-body fat was more accurately associated with the development of preeclampsia than was total body fat (33).

### Miscellaneous

Obesity during pregnancy is also associated with a slightly higher risk of urinary tract infections and thromboembolic disorders (1). On the other hand, anemia appears to occur less often in severely obese pregnant women than in normal-weight pregnant women (1, 14).
Prepregnancy BMI is a strong predictor of birth weight, and obese mothers deliver large-for-gestational-age infants 1.4 to 18 times more frequently than do lean mothers (6, 10–13, 15–18). Neonatal skinfold thickness is also higher in infants born to obese mothers, suggesting that the excess weight in the newborn is due to a larger fat mass (32). Macrosomia increases the risk for shoulder dystocia, birth injury, depression of Apgar scores, and perinatal death (36). Cesarean deliveries result in fewer birth injuries for macrosomic infants, but the perinatal death rate remains unchanged (37).

High gestational weight gain enhances the risk of delivering large-for-gestational-age infants in overweight women (6, 19). Gestational diabetes also affects fetal growth (36). However, the effect of gestational diabetes on birth weight can be counteracted by insulin treatment (28). In a multivariate analysis of 1000 mother-newborn pairs (209 with macrosomia), maternal constitutional factors predicted macrosomia better than positive OGTT results, and treated gestational diabetes was not a significant predictive factor (37). In patients with gestational diabetes, maternal weight is an independent risk factor that increases the risk of both macrosomia and operative delivery (38).

Fetal growth is also influenced by the location of body fat stores in the mother. The influence of regional distribution of fat on newborn size was investigated prospectively in a sample of 702 women whose preconceptional nutritional characteristics were recorded. Each 0.1-unit increase in pregravida waist-to-hip ratio predicted a 120-g greater birth weight, a 0.51-cm greater length, and a 0.3-cm greater head circumference (39).

### Congenital abnormalities

Maternal obesity is also a risk factor for congenital abnormalities. Data based on 56,857 children in an analysis from the National Institute of Neurological and Communicative Disorders and Stroke showed an increase in the incidence of major congenital malformations of 35% when mothers were overweight and of 37.5% when they were obese (3). This increase was later found to be accounted for by a higher percentage of neural tube defects; 4 independent studies reported an association between neural tube defects and maternal obesity (40–43). The odds ratios for neural tube defects in the offspring ranged from 1.8 to 2 according to the degree of maternal overweight (Table 3). This
relation persisted after adjustment for confounding factors such as maternal age, smoking, socioeconomic status, and folate intake. Obesity is also a risk factor for cryptorchism in male infants (adjusted odds ratio: 2.42; 95% CI: 1.11, 5.27) (44) and raises the risk of fluctuating dental asymmetry in the offspring, indicating developmental destabilization (45).

Mortality

Three cohort studies addressed the incidence of perinatal mortality according to the amount of pregravid weight excess (1, 3, 8). Even in moderately overweight mothers (BMI 25–30 or 120–150% of ideal body weight), the incidence of perinatal death in the infants was 1.15- to 2.5-fold higher than that in normal-weight women (1, 3). In obese women (BMI > 30 or > 150% of ideal body weight), the incidence of perinatal death in infants exceeded that in normal-weight women by 2.5 (3) and 3.4 (1). A more recent epidemiologic survey conducted in Sweden (8) reported that only late fetal deaths are significantly higher in overweight women (odds ratio: 1.7; 95% CI: 1.1, 2.4) and obese women (odds ratio: 2.7; 95% CI: 1.8, 4.1), whereas the risk for early neonatal death is not modified by maternal pregravid BMI (8). The effect of obesity is higher in nulliparous than in parous women (8). Maternal complications and preterm deliveries largely contribute to this excessive mortality (3).

LONG-TERM COMPLICATIONS

After delivery, obese mothers are more likely than normal-weight mothers to experience urinary symptoms such as stress incontinence and urgency (46). Excessive weight gain during pregnancy worsens maternal obesity. Weight gain during pregnancy is a strong predictor for sustained weight retention (47) and weight gains > 9 kg are correlated with the amount of weight retained between 2 successive pregnancies (48).

Infants of obese mothers are at higher risk of being overweight at 12 mo of age than are infants of normal-weight mothers (10). In particular, macrosomic infants are more likely to become obese in later life (49). When diabetes complicates the course of pregnancy, infants are predisposed to develop overweight and obesity during childhood, especially in the case of high birth weight (50). Hypertension during pregnancy is also responsible for increased morbidity during infancy. At 6 y of age, mean diastolic blood pressure is higher in children of women who developed preeclampsia during pregnancy than in children of children of control subjects (51).

However, a statistical association does not imply a causal relation. Genetic factors also play an important role in the development of obesity in the offspring of overweight mothers, as shown by Stunkard et al (52), who showed that the weight of adopted children correlated better with their natural parents’ weight than with that of their foster parents. A study from the Minnesota Twin Registry reported that in monozygotic twins, intrapair differences in birth weight correlate with intrapair differences in adult height but not with intrapair differences in adult BMI. Thus, intrauterine nongenetic factors (ie, environmental determinants of birth weight) influence adult height but not adult relative weight (53). This suggests that genetic factors are involved in the relation between maternal obesity and childhood obesity in the offspring.

COST

Despite the great number of surveys focused on pregnancy complications in overweight women, few data are available on the extra cost induced by these high-risk pregnancies. Considering the high prevalence of obesity among women of childbearing age, however, this is a major public health issue. In 1995 we found in a retrospective study that the cost of prenatal care in overweight women exceeded that in normal-weight control subjects by 5.4- to 16.2-fold depending on the degree of obesity (18). Because we wanted to control possible bias due to the retrospective design of our study, we also assessed the cost of pregnancy follow-up in a prospective case-control study.

We studied 435 pregnant women seen consecutively at the Obstetric and Gynecologic Department of Montpellier University Hospital in Montpellier, France, during the third trimester of their pregnancy and who gave their informed consent to participate in the study. The total duration of nighttime and daytime hospitalization in standard obstetric or surgical units during pregnancy and in the postpartum period was recorded. Fifty-four women (12.6%) had a BMI > 26 before becoming pregnant. Each was paired with a normal-weight control subject (BMI 18–25) matched for age and parity. Exclusion criteria were previous diabetes mellitus or severe disease, height < 145 cm, and age < 18 y. Forty-two case-control pairs who matched the inclusion criteria and whose anthropometric measurements and hospitalization records were complete were available for statistical analysis.

TABLE 3
Adjusted odd ratios (ORs) for neural tube defects in offspring of overweight mothers

<table>
<thead>
<tr>
<th>Reference</th>
<th>Mother’s BMI</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watkins et al (42)</td>
<td>&gt; 29</td>
<td>1.9 (1.1, 3.4)</td>
</tr>
<tr>
<td>Shaw et al (41)</td>
<td>&gt; 29</td>
<td>1.9 (1.3, 2.9)</td>
</tr>
<tr>
<td>Waller et al (40)</td>
<td>&gt; 31</td>
<td>1.8 (1.1, 3.0)</td>
</tr>
<tr>
<td>Werler et al (43)</td>
<td>&gt; 32</td>
<td>2.8 (1.1, 6.7)</td>
</tr>
<tr>
<td>Shaw et al (41)</td>
<td>31–37</td>
<td>1.5 (0.8, 2.7)</td>
</tr>
<tr>
<td>Waller et al (40)</td>
<td>31–37</td>
<td>1.8 (1.0, 3.2)</td>
</tr>
<tr>
<td>Shaw et al (41)</td>
<td>&gt; 38</td>
<td>2.6 (0.9, 7.7)</td>
</tr>
<tr>
<td>Waller et al (40)</td>
<td>&gt; 38</td>
<td>3.0 (1.2, 7.7)</td>
</tr>
</tbody>
</table>

TABLE 4
Hospital cost of pregnancy follow-up and delivery in overweight mothers

<table>
<thead>
<tr>
<th></th>
<th>Overweight women</th>
<th>Control women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>29.0 ± 5.5</td>
<td>29.0 ± 5.5</td>
</tr>
<tr>
<td>Parity</td>
<td>1.0 ± 1.1</td>
<td>1.0 ± 1.1</td>
</tr>
<tr>
<td>Pregravid BMI (kg/m²)</td>
<td>30.3 ± 4.02</td>
<td>20.8 ± 1.73²</td>
</tr>
<tr>
<td>Daytime hospitalization (d)</td>
<td>2.33 ± 2.60</td>
<td>0.60 ± 1.43³</td>
</tr>
<tr>
<td>Nighttime hospitalization (d)</td>
<td>2.55 ± 5.10</td>
<td>0.41 ± 1.22⁴</td>
</tr>
<tr>
<td>Cost of prenatal care (d)³</td>
<td>4.46 ± 5.97</td>
<td>0.89 ± 1.81⁶</td>
</tr>
<tr>
<td>Total cost (d)⁷</td>
<td>11.89 ± 7.29</td>
<td>7.46 ± 3.16⁸</td>
</tr>
</tbody>
</table>

² and ³Significantly different from overweight women, P = 0.001 (Student’s t test).³ and ⁴Significantly different from overweight women (Mann-Whitney-Wilcoxon test): ²P = 0.0001, ³P = 0.0237, ⁴P = 0.0002, ⁶P = 0.0019.
³Sum of duration of nighttime hospitalization and corrected daytime hospitalization.
⁴Sum of prenatal cost and corrected postpartum hospitalization.
TABLE 5
Admission of infants of normal-weight or overweight mothers to neonatal intensive care

<table>
<thead>
<tr>
<th>Reference</th>
<th>Normal weight</th>
<th>Overweight</th>
<th>Admission to neonatal intensive care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Normal weight</td>
</tr>
<tr>
<td>Perlow et al (16)</td>
<td>Weight &lt; 136 kg</td>
<td>Weight &gt; 136 kg</td>
<td>4.5</td>
</tr>
<tr>
<td>Galtier-Dereure et al (18)</td>
<td>18 &lt; BMI &lt; 25</td>
<td>BMI &gt; 30</td>
<td>9.3</td>
</tr>
<tr>
<td>Bianco et al (20)</td>
<td>19 &lt; BMI &lt; 27</td>
<td>BMI &gt; 35</td>
<td>8.7</td>
</tr>
</tbody>
</table>

*1–3Significantly different from normal weight: 1 P < 0.01, 2 P < 0.001, 3P < 0.01.*

The cost of hospitalization was calculated as described previously (18). Briefly, the cost was expressed in days of hospitalization in a nighttime obstetric department. When women were hospitalized in units where the daily price differed, a correcting coefficient was applied: 0.766 for daytime hospitalization and 1.40 for nighttime hospitalization in a surgical department (in the case of cesarean delivery). The cost of prenatal care was the sum of the duration of nighttime hospitalization and corrected daytime hospitalization. The total cost was the sum of the cost per day and corrected postpartum hospitalization. The hypothesis that no difference existed between means was evaluated with Student’s t test or the Mann-Whitney-Wilcoxon test when appropriate. Results were considered significant if the P value was < 0.05.

As shown in Table 4, the average cost of hospital prenatal care was 5 times higher in mothers who were overweight before pregnancy than in normal-weight control women. The duration of both day and night hospitalization was also higher, by 3.9- and 6.2-fold, respectively. When both pre- and postnatal care were considered, women whose pregravid BMI was > 29 stayed in the hospital an average of 4.43 more days than did lean women. Thus, these results emphasize that maternal weight excess has a high cost.

The percentage of infants requiring admission to a neonatal intensive care unit is 3.5 times higher in cases of maternal obesity (16, 18, 20) (Table 5). Obesity also leads to significantly longer postpartum hospital stays as a result of more frequent cesarean deliveries and endometritis (54). The long-term social and economic effects of maternal obesity-related birth trauma, neural tube defects, and childhood obesity were not evaluated.

MANAGEMENT

Preconception counseling

Overweight women of childbearing age should be informed of the risks associated with pregnancy and receive appropriate dietary counseling. These women should be screened for hypertension and carbohydrate intolerance and encouraged to perform physical activity. Stable, massive pregravid weight loss in morbidly obese women markedly reduces the occurrence of maternal complications during pregnancy (55).

Optimal weight gain in obese pregnant women

How much weight obese women should gain during pregnancy is controversial. In this case, maternal and fetal interests seem to be in conflict. The Institute of Medicine recommends a minimum increase of 6.8 kg even for massively obese women to improve fetal outcome (56). But gestational weight gain appears to benefit maternal fat stores rather than birth weight in obese women. Each kilogram of gestational weight gain increases birth weight by 44.9 g for very underweight women, by 22.9 g for normal-weight women, and by 11.9 g for overweight women (57). Although an association between low weight gain and low birth weight in obese women is sometimes reported (19), most studies fail to show any association (2, 6, 20). In a recent study involving 53,541 live births, the odds ratio for delivering low-birth-weight infants when weight gains were < 6.8 kg in overweight (BMI 26–29) and very overweight (BMI > 29) mothers and overweight women was not statistically significant (6). On the other hand, high weight gains in overweight and obese mothers lead to a higher rate of macrosomic infants (6, 19, 20). Moreover, low weight gains are associated with lower weight retention after birth and fewer long-term complications of obesity (47, 48). To date, no study has simultaneously considered fetal outcome and long-term maternal complications associated with different categories of weight gain in obese pregnancies.

Postpartum

Birth-control methods must be chosen according to maternal relative weight and possible concomitant metabolic or vascular disorders. Women in whom gestational diabetes is diagnosed must be screened for type 2 diabetes 2 mo after delivery or after the end of lactation. Prevention of future overt type 2 diabetes is a major issue in these patients.

CONCLUSION

Even moderate overweight has a significant deleterious effect on the outcome of pregnancy, and obesity leads to major maternal and fetal complications. Given the major economic and medical consequences of pregnancy in overweight women, all attempts should be made to prevent obesity in women of childbearing age and to encourage weight loss before pregnancy. The consequences of obesity on maternal and fetal morbidity and mortality might be minimized through appropriate multidisciplinary management.

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REFERENCES


