# Bipolar History Linked to Depression in Pregnancy

*Women with a history of unipolar depression or bipolar disorder at risk for peripartum, postpartum depression.*

BY MITCHEL L. ZOLER
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PITTSBURGH — Women with a history of bipolar disorder have an increased risk of developing depression during and after pregnancy, based on a review of more than 2,000 pregnant women.

A history of unipolar depression also predisposed women to develop depression during the peripartum and postpartum periods, although unipolar depression was not as potent a risk factor as bipolar disorder. The findings suggest "an urgent need" for better screening and detection of bipolar-spectrum disorders in pregnant women, Adele C. Viguera, M.D., said while presenting a poster at the Sixth International Conference on Bipolar Disorders.

The results show that pregnant women with a history of bipolar disorder or unipolar depression are "ticking time bombs" for the development of peripartum or postpartum depression, Dr. Viguera, associate director of perinatal and reproductive psychiatry at Massachusetts General Hospital, Boston, told this newspaper.

Women with bipolar disorder who are treated with lithium while breast-feeding transfer a modest amount of lithium to their infant children. "Adverse clinical effects in infants exposed to lithium through breast milk were rare and clinically insignificant" in a study with 10 mother-infant pairs, Dr. Viguera reported in a second poster at the conference, which was sponsored by the University of Pittsburgh.

The prevalence of bipolar depression in pregnant women and its association with peripartum and postpartum depression was assessed in 2,340 consecutive women who sought prenatal care at the Massachusetts General Hospital during 1996-1999.

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A mood-disorder questionnaire was completed by 1,814 of the study participants during their second trimester, and 526 women completed a second questionnaire when they were seen at the clinic 6 weeks after delivery.

Bipolar disorder was diagnosed in women with a self-reported history of mania with or without a history of depression. Depression during pregnancy or the postpartum period was diagnosed when women scored at least 16 on the Center for Epidemiologic Studies Depression Scale.

The average age of the entire group of 2,340 women was 32.5 years, and 61% did not have children before the index pregnancy.

The women who finished their pregnancy questionnaires had a 3.2% overall prevalence of probable bipolar disorder at some time during their lives.

In the second trimester, the prevalence of depression was about 52% among women with a history of bipolar disorder, about 34% among those with a history of unipolar depression, and about 8% among women with no history of a mood disorder. The differences between the bipolar and unipolar groups and the women with no mood disorders were statistically significant, Dr. Viguera reported.

At the sixth week post partum, the prevalence of depression was 50% among women with a history of bipolar disorder, about 32% among women with a history of unipolar depression, and about 6% among women with no history of mood disorders. Again, the prevalence of depression was significantly greater among women with a history of bipolar disorder or unipolar depression, compared with those who did not have this history.

During and after pregnancy, depression should be closely monitored, especially in women with a history of depression or bipolar disorder. These women can be treated like any other patients with these disorders, Dr. Viguera said. Patients with bipolar disorder should receive a mood stabilizer, while those with unipolar depression should get an antidepressant.

The passage of lithium from mother to child via breast milk was examined in a separate study that involved 10 mother-infant pairs. Serum and breast milk samples were obtained from both the mothers and infants at 4-12 weeks' post partum, both before a dose of lithium was administered and within 12 hours after a dose. Repeat samples were collected from five subjects.

The average maternal dose of lithium was 850 mg/day, which led to an average serum concentration of 0.76 mEq/L. The average lithium concentration in milk was 0.35 mEq/L, and the average serum level in the infants was 0.16 mEq/L.

The findings suggest a "rule of halves" for lithium: Breast milk contains about half the lithium concentration as maternal serum, and infant serum contains about half of the concentration in breast milk, Dr. Viguera said. (This means that infant serum contains about one-fourth the concentration in maternal serum.)

Nine of the 10 infants in the study showed no adverse effects from lithium exposure. One infant had an elevated level of TSH, but the level normalized within 2 weeks after lithium was stopped. All of the other nine infants had TSH levels that were within the normal range. Renal function was normal for all 10 infants, and there were no other acute effects seen. Follow-up observations and reports also showed no late developmental abnormalities.

In routine practice, infants who are nursed by mothers treated with lithium should be monitored by serum assays of TSH, blood urea nitrogen, and serum creatinine every 6-8 weeks during breast-feeding, Dr. Viguera said. ■

# Treatment of GDM Reduces Perinatal Morbidity, Study Suggests

BY MIRIAM E. TUCKER
*Senior Writer*

Treatment of gestational diabetes reduces serious perinatal morbidity, Caroline A. Crowther, M.D., of the University of Adelaide (Australia) and her associates reported.

Although the risks associated with gestational diabetes mellitus (GDM) are well recognized, it has been uncertain whether screening and treatment to reduce maternal glucose levels reduces these risks. Given this uncertainty, professional groups disagree on which patients should be screened, the investigators said (N. Engl. J. Med. 2005;352:2477-86).

Now, new investigation findings in favor of screening come from the 18-center Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) in which serious perinatal complications occurred in just 1% of the infants of 490 women with GDM who were randomized to intensive glucose management, compared with 4% of 510 women who received routine care.

In an accompanying editorial, Michael F. Greene, M.D., and Caren G. Solomon, M.D., wrote that "this study provides critical evidence that identifying and treating [GDM] can substantially reduce the risk of adverse perinatal outcomes without, at least in this trial, increasing the rate of cesarean delivery."

However, Dr. Greene and Dr. Solomon, both on the editorial board of the New England Journal of Medicine, noted that the study leaves unanswered the question of what level of blood glucose warrants routine intervention (N. Engl. J. Med. 2005;352:2544-6).

The study included women with a singleton or twin pregnancy between 16 and 30 weeks' gestation who had at least one risk factor for GDM on selective screening or a positive 50-g oral glucose challenge test, with a 1-hour postchallenge glucose level of at least 140 mg/dL followed by a 75-g oral glucose tolerance test at 24-34 weeks' gestation in which venous plasma glucose was less than 140 mg/dL after an overnight fast and 140-198 mg/dL at 2 hours.

When the study began, these women had been classified as having glucose intolerance of pregnancy by the World Health Organization, but during the course of the study (in 1998) WHO began classifying any glucose level above normal as being GDM. Women whose glucose values exceeded these cutoffs were not included in the study.

The women randomized to intensive intervention were informed of their diagnosis. They received dietary counseling and were taught how to perform self–blood glucose monitoring, with targets of no more than 99 mg/dL premeal and 126 mg/dL 2 hours after eating. Twenty percent received insulin therapy. The women randomized to routine care were told they did not have GDM, according to Dr. Crowther and her associates.

Serious perinatal outcomes, including death, shoulder dystocia, bone fracture, and nerve palsy, occurred in 1% of the intervention group vs. 4% of the routine care group after adjustment for maternal age, race/ethnicity, and parity. Thus, 34 mothers would need to be treated to prevent one serious outcome in an infant, they said.

Women in the intervention group were significantly more likely to have induction of labor (39% vs. 29%), but the rates of cesarean delivery were similar (31% vs. 32%), as were the reasons for it. Infants in the intervention group also had fewer admissions to the neonatal nursery (71% vs. 61%). At 3 months' post partum, fewer women in the intervention group had a score on the Edinburgh Postnatal Depression Scale suggestive of depression (8% vs. 17%); anxiety scores were similar.

Among the secondary outcomes, there were no perinatal deaths among the infants from the intervention group, but three stillbirths and two neonatal deaths occurred among infants in the routine care group. There were no differences in the rates of shoulder dystocia between the two groups. No bone fractures or nerve palsies occurred in the intervention group; the routine care group had one of the former and three of the latter.

Birth weights were significantly lower among the infants born to women in the intervention group (3,335 g vs. 3,482 g), and they were also born at an earlier gestational age, which makes sense given their higher rate of induction of labor. Significantly fewer infants in the intervention group were large for gestational age (13% vs. 22%), and fewer had macrosomia, defined by a birth weight of 4 kg or greater (10% vs. 21%).

Women in the intervention group made fewer prenatal clinic visits after enrollment than did the routine care group, but they made more visits to the physician. Weight gain was less in the intervention group, and fewer women were diagnosed with preeclampsia. The rates of prenatal hospital admissions were similar.

Dr. Greene and Dr. Solomon agreed with the authors' justification for having randomized one group of women to no treatment—that before this study there were no conclusive data regarding the effects of treating GDM, even after the WHO definition was revised. ■

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