American Journal of Epidemiology
Vol. 159, No. 9
Printed in U.S.A.
DOI: 10.1093/aje/kwh122

Neonatal Outcome following Maternal Antenatal Depression and Anxiety: A Population-based Study

Liselott Andersson[1,2], Inger Sundström-Poromaa[3], Marianne Wulff[1], Monica Åström[4], and Marie Bixo[1]

[1] Department of Clinical Sciences, Division of Obstetrics and Gynecology, Umeå University, Umeå, Sweden.
[2] Department of Obstetrics and Gynecology, Sunderby Hospital, Luleå, Sweden.
[3] Department of Women's and Children's Health, University Hospital, Uppsala, Sweden.
[4] Department of Clinical Sciences, Division of Psychiatry, Umeå University, Umeå, Sweden.

Received for publication September 22, 2003; accepted for publication December 3, 2003.

The aim of this study was to determine neonatal outcomes among women who had depressive and anxiety disorders during the second trimester of pregnancy in a population-based sample. Participants were 1,465 women and their neonates born at two obstetric clinics in Sweden. The inclusion period for the women was October 2, 2000–October 1, 2001. The Primary Care Evaluation of Mental Disorders (PRIME-MD) classification system was used to evaluate mental disorders in the second trimester of pregnancy. For assessment of demographic characteristics, birth statistics, and birth-related complications, the medical records of the included women and their offspring were reviewed after delivery. The study results revealed no differences in neonatal outcome between women with antenatal depressive disorders and/or anxiety disorders and healthy subjects. The authors conclude that neonatal outcome did not deteriorate despite the women's impaired mental health during pregnancy.

anxiety; depression; pregnancy

Abbreviations: CI, confidence interval; CES-D [Scale], Center for Epidemiologic Studies Depression [Scale]; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; OR, odds ratio; PRIME-MD, Primary Care Evaluation of Mental Disorders.

Prior studies have indicated that depression and anxiety during pregnancy affect neonatal outcome. In particular, attention has focused on the increased risks of spontaneous preterm delivery, low birth weight, operative delivery (cesarean section and instrumental vaginal delivery), and admission to a neonatal intensive care unit among offspring of women with antenatal depression (1–3). Not only does depression tend to shorten pregnancy but major life events, if they are perceived as stressful, tend to shorten it as well (4, 5). Antenatal stress has been suggested to cause preterm delivery through activation of the placental-maternal pituitary-adrenal axis (6). This hypothesis is further supported by a relation between preterm birth and elevated levels of corticotropin-releasing hormone in maternal plasma and in placenta (6–8). On the other hand, a number of Scandinavian studies have reported that maternal psychological distress does not seem to influence fetal growth (9, 10).

Although a number of studies have indicated a relation between maternal antenatal depression and/or anxiety and neonatal outcome, few population-based studies have investigated the issue. Most previous studies have been performed with small samples, mainly in specific risk groups such as teenage mothers, women of low socioeconomic status, and women of certain ethnic groups (1, 11, 12). In addition, there has been a deficit of studies on antenatal depression and/or anxiety using diagnostic criteria adhering to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) (13). The aim of this study was to investigate neonatal outcome in an unselected population-based sample of pregnant women diagnosed with antenatal depressive and/or anxiety disorders in comparison with healthy mothers. In

Correspondence to Dr. Liselott Andersson, Department of Obstetrics and Gynecology, Sunderby Hospital, S-97180 Luleå, Sweden (e-mail: liselott.andersson@nll.se).

the light of previous study results, the main hypothesis was that there would be associations between antenatal depression and/or anxiety and adverse neonatal outcome in terms of spontaneous preterm delivery and/or small-for-gestational-age birth.

MATERIALS AND METHODS

Study population

All women undergoing routine second-trimester ultrasound screening at Umeå University Hospital and at Sunderby Central Hospital were approached for study participation. The study period lasted 1 year, from October 2, 2000, to October 1, 2001. In Sweden, all pregnant women are invited to undergo ultrasound examination at 16–18 weeks of gestation for estimation of the date of childbirth. No other methods are used to assess duration of gestation in spontaneous pregnancies. Approximately 97 percent of pregnant Swedish women participate (14). During the study period, Umeå University Hospital served a population of 134,428 people, of whom 27,063 were women of reproductive age. The corresponding figures for Sunderby Central Hospital were 115,600 and 19,277, respectively. Most important, there were no other available ultrasound screening facilities or delivery departments in these two cities.

Exclusion criteria for the original study were 1) detection of a malformation or missed spontaneous abortion at the ultrasound examination, 2) inability to read and understand the questionnaire because of language difficulties, and 3) not providing informed consent. Furthermore, in the present study, only singletons, livebirths, and subjects with complete medical records regarding the newborns were included. Use of psychoactive medication during pregnancy was not an exclusion criterion.

Psychiatric diagnosis

Psychiatric disorders were diagnosed using the Primary Care Evaluation of Mental Disorders (PRIME-MD) classification system (15). The PRIME-MD system conforms to DSM-IV criteria and has been validated for use in primary care settings. Agreement between PRIME-MD diagnoses and those of independent mental health professionals is excellent, with a sensitivity of 83 percent, a specificity of 88 percent, a positive predictive value of 80 percent, and an overall accuracy of 88 percent (15). Given its utility and ease of use, we considered PRIME-MD to be a suitable tool for assessing the prevalence of psychiatric disorders in an obstetric outpatient setting. The PRIME-MD system, which is fully described elsewhere (15), consists of two components: a one-page patient questionnaire and a 12-page clinician evaluation guide, which is a structured interview for the clinician to follow when evaluating responses on the patient questionnaire. The original clinician evaluation guide contained modules for mood, anxiety, and eating disorders, alcohol abuse, social phobia, and obsessive-compulsive disorder. Clinicians administer only those modules that are indicated by the patient on the patient questionnaire.

The PRIME-MD system evaluates the presence of 20 possible mental disorders; this study focused on 13 diagnoses of interest. Among these 13 diagnoses, eight correspond to the specific requirements of the DSM-IV (major depressive disorder, dysthymia, partial remission of major depressive disorder, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, social phobia, and bulimia nervosa). An additional four diagnoses are considered to be "subthreshold" diagnoses, such as minor depressive disorder, anxiety not otherwise specified, eating disorder not otherwise specified, and binge eating disorder. Subthreshold diagnoses have fewer symptoms than are required for a specific DSM-IV diagnosis but were included because they are associated with considerable impairment in function (16). Finally, a rule-out diagnosis of bipolar disorder was included. A modified form of the PRIME-MD patient questionnaire was used for this study. It contained 25 questions evaluating somatoform disorder, mood disorders, anxiety disorders (including social phobia and obsessive-compulsive disorder), and eating disorders. Somatoform disorders, alcohol abuse, and rule-out diagnoses of mood disorder and/or anxiety due to physical disorder, medication use, or drug use were not assessed.

Study design

The women completed the PRIME-MD patient questionnaire before attending the ultrasound examination. Along with the patient questionnaire, they were asked to provide their name, date of birth, and telephone number and an informed consent statement allowing for a telephone interview. If any key question indicated a mental disorder, the woman was considered screen-positive, and a telephone interview was conducted within 1–2 weeks after the ultrasound examination, using a computerized version of the clinician evaluation guide. Women who received a PRIME-MD diagnosis and also were asking for help and/or had thoughts about committing suicide were immediately referred to a psychiatric specialist. One research nurse and four obstetricians performed the telephone interviews.

Three months after delivery, the medical records of the women and their offspring were thoroughly reviewed. Only cases with complete medical records, livebirths, and singleton pregnancies were included in the study. The reason for the inclusion of only singletons was that infants from multiple births are well known to be at greater risk of preterm birth and deteriorated fetal growth (17).

The main results are fully described elsewhere (18). A total of 2,263 women were examined by ultrasound screening during the inclusion period. After exclusions due to refusal to participate (10 women), language difficulties (82 women), excess numbers of patients (362 women), and other factors (14 women), 1,795 women received the PRIME-MD patient questionnaire. Sixty-four women did not answer the questionnaire, and 105 did not sign the informed consent form. A further 22 women were excluded because of missed spontaneous abortion or malformation, and 49 could not be reached within the stipulated 14 days. Complete medical records regarding the newborns were retrieved for 1,492 subjects. These 1,492 women delivered

1,513 children. Six children were excluded because of stillbirth, and 42 twins were removed from the analyses, leaving a total of 1,465 children.

From the medical records of the mothers, data on age, parity, body mass index in the first trimester, marital status, socioeconomic status, smoking and tobacco use, alcohol consumption, and the prevalence of chronic disease were extracted. Data on birth length, birth weight, pH of and base deficit in umbilical artery blood, Apgar score at 1 and 5 minutes, neonatal intensive care, and the most common pediatric diagnoses were recorded from the pediatric medical charts. The diagnoses recorded for the study were overall preterm birth, spontaneous preterm birth, small-for-gestational-age birth, respiratory distress, asphyxia, and malformation. Pediatricians examined and diagnosed the newborns during the hospital stay postpartum.

The study was approved by the Ethics Committee of Umeå University, Umeå, Sweden.

Statistical analyses

A comparison regarding overall preterm delivery was made between the study population of 1,465 women and the 755 women who were not included in the study group. The latter group consisted of nonresponders (n = 179) and the 576 women who did not meet the criteria for inclusion in the study after removal of twins (n = 12) and stillbirths (n = 4). Frequencies were compared between groups by means of the chi-squared test.

The study was designed to detect an increase in the rate of overall premature births from 6 percent to 12 percent in women with depressive and/or anxiety disorders compared with controls ($\alpha = 0.05$, $\beta = 0.20$). Bivariate logistic regression analysis was used to compute odds ratios for neonatal outcome in terms of birth weight, small-for-gestational-age birth, overall preterm birth, and spontaneous preterm birth. Adjusted odds ratios for all variables regarding neonatal outcome were computed using a multiple logistic regression model, which included possible maternal confounding factors and mediators, selected according to prior studies (1).

Maternal confounders and mediators were defined as follows: maternal age as completed years of age at the time of the psychiatric investigation; parity as primiparity or parity of one or more; marital status as being married to/cohabiting with the father of the child or single parenting; and socioeconomic status as professional employee or laborer, according to Swedish socioeconomic indices. Smoking status was recorded at the first antenatal care visit and was categorized into nonsmoking (not daily smoking), smoking of 1–9 cigarettes per day, and smoking of 10 or more cigarettes per day. Likewise, oral use of finely ground tobacco was categorized into nonuse and use. First-trimester body mass index (weight (kg)/height $(m)^2$) was categorized according to the recommendation of the World Health Organization: underweight (body mass index <18.5), normal (body mass index 18.5–24.9), overweight (body mass index 25.0–29.9), and obese (body mass index ≥30). Chronic diseases were considered prevalent when a history of heart disease, diabetes mellitus, hypertension, or renal disease was recorded at the first antenatal visit.

Neonatal variables were categorized accordingly. Birth weight was categorized into <2,500 g, 2,500–3,999 g, and ≥4,000 g. The values of umbilical artery blood pH below 7.2 and/or base deficit lower than –12 mmol/liter were used as biochemical markers for acidosis. Apgar scores below 4 points 1 and/or 5 minutes after birth were regarded as indicating established asphyxia in the analyses. Preterm births were divided into two groups because the overall rate of preterm delivery is partly medically determined, as in cases with severe complications that threaten the fetus and/or mother. In this study, the traditional cutoff point of less than 37 weeks of completed gestation was used as the definition of preterm delivery. Gestational age was estimated according to the result of the second-trimester ultrasound screening. No other methods were used in spontaneous pregnancies. Gestational age in pregnancies resulting from in vitro fertilization was estimated according to the day of embryo transfer. Spontaneous preterm birth was defined as rupture of membranes and/or premature labor before 37 completed weeks of gestation. The division into separate groups was supported by results from prior studies suggesting that preterm birth comprises etiologically distinct categories (19, 20).

Small-for-gestational-age birth was defined as birth weight below the 2.5th percentile for expected weight according to gestational age. In Sweden, in 2001, the mean birth weight was 3,629 g for boys and 3,505 g for girls.

All statistical analyses were performed using SPSS for Windows, version 10.0 (SPSS, Inc., Chicago, Illinois). A two-sided p value less than 0.05 was considered significant.

RESULTS

Study population

A total of 1,465 women were included, 204 (13.9 percent) with a PRIME-MD diagnosis and 1,261 (86.1 percent) without any diagnosis. Depressive disorders were present in 170 cases (11.6 percent) and thus were the most common. Major depressive disorder was present in 46 women (3.1 percent), and 104 women (7.1 percent) had minor depression. Anxiety disorders were present in 86 women (5.9 percent); anxiety not otherwise specified was the most common, found in 60 cases (4.1 percent). Obsessive-compulsive disorder was diagnosed in 16 women (1.1 percent), social phobia in six (0.4 percent), and eating disorders in three (0.2 percent).

Eleven (5.4 percent) of the 204 women with a PRIME-MD diagnosis received some sort of treatment for their psychiatric condition. Only one of them was using antidepressant medication at the time of the second-trimester ultrasound screening. One additional woman was prescribed antidepressant medication later in pregnancy. In both of these cases, the drug taken was a selective serotonin reuptake inhibitor. None of the women without a PRIME-MD diagnosis were noted to use psychoactive medication. Prepregnancy use of antidepressant medication was noted in 18 women (1.2 percent). However, all women taking antidepressant medication prior to pregnancy had withdrawn from it prior to the first midwife visit.

Neonatal outcome

Comparison between the women who were not included in the study (excluded subjects and nonresponders) and the study population revealed no significant differences regarding overall preterm births. The number of preterm births was 26 (4.3 percent) among women not included in the study group and 76 (5.2 percent) in the study population (p = 0.44). Among women not included, data were missing for 149 subjects.

The bivariate unadjusted analysis revealed no significant associations between any antenatal PRIME-MD diagnosis and deteriorated neonatal outcome (birth weight <2,500 g: odds ratio (OR) = 1.41 (95 percent confidence interval (CI): 0.58, 3.49); birth weight ≥4,000 g: OR = 1.32 (95 percent CI: 0.94, 1.88); small-for-gestational-age birth: OR = 0.68 (95 percent CI: 0.16, 2.97); overall preterm birth: OR = 1.05 (95 percent CI: 0.54, 2.02); spontaneous preterm birth: OR = 0.83 (95 percent CI: 0.32, 2.14)). A borderline-significant bivariate association between antenatal depressive disorder and increased birth weight was revealed (birth weight <2,500 g: OR = 1.20 (95 percent CI: 0.41, 3.48); birth weight ≥4,000 g: OR = 1.45 (95 percent CI: 1.00, 2.10); small-for-gestational-age birth: OR = 0.01 (95 percent CI not calculated); overall preterm birth: OR = 1.32 (95 percent CI: 0.68, 2.56); spontaneous preterm birth: OR = 1.04 (95 percent CI: 0.40, 2.69)). Finally, no significant bivariate associations were found between antenatal anxiety disorder and neonatal outcome (birth weight <2,500 g: OR = 1.45 (95 percent CI: 0.34, 6.26); birth weight ≥4,000 g: OR = 1.11 (95 percent CI: 0.60, 2.05); small-for-gestational-age birth: OR = 2.23 (95 percent CI: 0.51, 9.82); overall preterm birth: OR = 0.90 (95 percent CI: 0.28, 2.96); spontaneous preterm birth: OR = 0.52 (95 percent CI: 0.07, 3.89)).

The distribution of potential maternal confounding factors and mediators for psychiatric disorders is presented in table 1. Significant associations with a PRIME-MD diagnosis were observed for not being married or cohabiting, low socioeconomic status, smoking 10 or more cigarettes daily, or having a body mass index of 30 or more. The relations of neonatal outcome to any PRIME-MD diagnosis, any depressive disorder, and any anxiety disorder are shown in tables 2, 3, and 4, respectively. There were no significant differences in any of the studied variables between the newborns of women with a depressive and/or anxiety disorder and the newborns of women without a diagnosis (table 2). Newborns of women with exclusively depressive disorders (major depressive disorder, dysthymia, partial remission of major depressive disorder, minor depressive disorder, and bipolar disorder) did not differ significantly from newborns of women without a diagnosis (table 3). As table 4 shows, there were no significant differences between the newborns of healthy women and the newborns of women with anxiety disorders (anxiety not otherwise specified, generalized anxiety, panic disorder, obsessive-compulsive disorder, and social phobia).

DISCUSSION

The findings of the present study suggest that neonatal outcome does not deteriorate because of maternal antenatal depressive and/or anxiety disorders. Although our results contradict the findings of previous studies (1–3), the present study is unique in being based on an unselected population-based sample of women and using modern DSM-IV criteria for psychiatric diagnosis.

Orr et al. (1) found a significant relation between spontaneous preterm delivery and reported depressive symptoms. A major reason for the divergent results might be that both aims and diagnostic instruments differed between studies, since Orr et al. used the Center for Epidemiologic Studies Depression (CES-D) Scale for assessment of depressive symptoms, not depression as a clinical diagnosis. In their study, 117 (8.4 percent) of the women had a CES-D score in the upper 10th percentile. The prevalence of depressive disorders diagnosed according to PRIME-MD in our study was 11.6 percent, and major depression was present in 46 women (3.1 percent). Besides the use of different methods, another possible reason for the diverse results might be that the populations were different and that the risk of premature birth differs considerably between continents. Premature birth per se is about twice as common in the United States as in Sweden (21, 22), with point prevalences of 12.0 percent and 5.7 percent, respectively. Our data on premature birth correspond well with the reported number of premature births in Sweden, in its entirety. The population in the study by Orr et al. (1) consisted of African-American women, who are already known to be at greater risk of preterm delivery than White women (23, 24). One explanation offered is that US Black women are chronically exposed to specific stressors that adversely affect pregnancy outcome and that race is a marker for that stress but not in itself a risk factor for preterm delivery (23).

Kelly et al. (25) found independent associations between maternal psychiatric and substance abuse diagnoses and low birth weight and preterm delivery in an ethnically heterogeneous population in California. Psychiatric and substance use diagnoses were retrospectively determined by means of *International Classification of Diseases, Ninth Revision, Clinical Modification,* diagnostic codes recorded on the maternal hospital discharge summary. In women with a psychiatric diagnosis, the adjusted odds ratio for low birth weight (<2,500 g) was 2.0 (95 percent CI: 1.7, 2.3). For preterm delivery, the adjusted odds ratio was 1.6 (95 percent CI: 1.4, 1.9). However, one of the study limitations noted by those authors was the possibility that unmeasured confounders, such as maternal smoking, could have biased the risk estimates.

Two studies on a large Danish population found no relation between elevated distress scores and fetal growth retardation (9) but revealed a moderate relation between elevated distress scores and preterm delivery (26). Women who experienced one or more highly stressful life events during pregnancy had an odds ratio of 1.76 for preterm delivery (95 percent CI: 1.15, 2.71). Again, however, these two studies assessed depression and anxiety not as clinical diagnoses but rather as scores for distress symptoms.

TABLE 1. Assocation of selected demographic, behavioral, and medical characteristics with a PRIME-MD† diagnosis during the second trimester of pregnancy, Umeå University Hospital and Sunderby Central Hospital, Sweden, January 2000–January 2001

Variable	PRIME-MD diagnosis (exposed) (n = 204)‡		No PRIME-MD diagnosis (unexposed) (n = 1,261)‡		Odds ratio	95% confidence interval
	No.	%	No.	%		
Age (years)						
≤19	5	2.5	22	1.7	1.08	0.37, 3.15
20–29	90	44.1	606	48.1	1.00§	
30–39	106	52.0	616	48.9	1.21	0.86, 1.71
≥40	3	1.5	17	1.3	1.54	0.43, 5.53
Marital status**						
Married or cohabiting	186	91.2	1,221	97.4	1.00§	
Not married or cohabiting	18	8.8	33	2.6	2.74	1.38, 5.43
Socioeconomic status*						
Professional employee	60	29.4	504	40.4	1.00§	
Laborer	144	70.6	743	59.6	1.51	1.06, 2.16
Smoking*						
Nonsmoker	178	87.7	1,174	93.9	1.00§	
Cigarette smoker (cigarettes/day)						
1–9	15	7.4	55	4.4	1.50	0.80, 2.83
≥10	10	4.9	21	1.7	2.53	1.13, 5.70
Use of tobacco other than cigarettes						
Nonuser	191	94.1	1,177	94.2	1.00§	
Tobacco user	12	5.9	73	5.8	1.09	0.57, 2.08
Parity						
1	76	37.3	561	44.5	1.00§	
≥1	128	62.7	699	55.5	1.27	0.90, 1.80
Alcohol consumption						
Rarely or never drank alcohol	203	99.5	1,248	99.9	1.00§	
Drank alcohol	1	0.5	1	0.1	0.01	—¶
Chronic disease						
No	198	97.1	1,229	97.9	1.00§	
Yes	6	2.9	27	2.1	1.08	0.40, 2.96
First-trimester body mass index*,#						
<18.5	4	2.1	21	1.8	1.13	0.36, 3.47
18.5–24.9	106	54.9	728	61.7	1.00§	
25.0–29.9	51	26.4	323	27.4	1.04	0.72, 1.50
≥30.0	32	16.6	108	9.2	1.70	1.07, 2.70

* $p < 0.05$; ** $p < 0.01$.

† PRIME-MD, Primary Care Evaluation of Mental Disorders.

‡ Data on the body mass index variable were missing for 93 (6.3%) women. For the variables marital status, socioeconomic status, smoking, tobacco use (other than cigarette smoking), alcohol consumption, and chronic disease, the prevalence of missing data was 0.1–1.0%.

§ Referent.

¶ Not calculated.

Weight (kg)/height (m)^2.

Hoffman and Hatch (3) pointed out a possible association between prenatal depressive symptoms at 28 weeks of gestation and deteriorated fetal growth in 222 women of lower social class, raising questions as to whether being of a lower social class is a vulnerability factor per se. In their study, CES-D scores were used for assessment of depressive symptoms in 666 women. They did not find any associations between depressive scores and adverse neonatal outcomes in

TABLE 2. Neonatal outcome according to the prevalence of antenatal PRIME-MD* diagnosis, Umeå University Hospital and Sunderby Central Hospital, Sweden, January 2000–January 2001

Variable	PRIME-MD diagnosis (exposed) (n = 204)†		No PRIME-MD diagnosis (unexposed) (n = 1,261)†		Adjusted odds ratio‡	95% confidence interval
	No.	%	No.	%		
Birth weight (g)						
<2,500	6	2.9	28	2.2	1.47	0.58, 3.70
2,500–3,999	147	72.1	974	77.5	1.00§	
≥4,000	51	25.0	255	20.3	1.26	0.86, 1.84
Umbilical artery pH						
≥7.2	139	81.8	883	83.5	1.00§	
<7.2	31	18.2	174	16.5	1.17	0.75, 1.83
Umbilical artery base deficit (mmol/liter)						
≥–12	165	99.4	1,012	98.2	1.00§	
<–12	1	0.6	19	1.8	0.42	0.05, 3.19
Apgar score at 1 minute						
≥4	201	98.5	1,240	98.8	1.00§	
<4	3	1.5	15	1.2	1.51	0.43, 5.30
Apgar score at 5 minutes						
≥4	204	100	1,251	99.7	1.00§	
<4	0		4	0.3	0.04	—¶
Neonatal intensive care						
No	184	90.2	1,113	88.3	1.00§	
Yes	20	9.8	147	11.7	0.84	0.50, 1.42
Overall premature birth						
No	193	94.6	1,196	94.8	1.00§	
Yes	11	5.4	65	5.2	0.96	0.47, 1.92
Spontaneous premature birth						
No	199	97.5	1,224	97.1	1.00§	
Yes	5	2.5	37	2.9	0.74	0.26, 2.12
Small-for-gestational-age birth						
No	202	99.0	1,243	98.6	1.00§	
Yes	2	1.0	18	1.4	0.52	0.11, 2.41
Respiratory distress						
No	199	97.5	1,225	97.1	1.00§	
Yes	5	2.5	36	2.9	0.98	0.37, 2.60
Asphyxia						
No	201	98.5	1,251	99.2	1.00§	
Yes	3	1.5	10	0.8	2.14	0.58, 7.96
Malformation						
No	203	99.5	1,238	98.2	1.00§	
Yes	1	0.5	23	1.8	0.25	0.03, 1.93

* PRIME-MD, Primary Care Evaluation of Mental Disorders.

† Data on the base deficit variable were missing for 268 newborns (18.3%), and data on the pH variable were missing for 238 newborns (16.2%). For the variables birth weight, neonatal intensive care, and Apgar score at 1 and 5 minutes, the prevalence of missing data was 0.1–0.4%.

‡ Odds ratios were adjusted for age, marital status, socioeconomic status, smoking habits, and body mass index.

§ Referent.

¶ Not calculated.

TABLE 3. Neonatal outcome according to the prevalence of antenatal mood disorder, Umeå University Hospital and Sunderby Central Hospital, Sweden, January 2000–January 2001

Variable	Antenatal mood disorder (exposed) (n = 164)*		No antenatal mood disorder (unexposed) (n = 1,261)*		Adjusted odds ratio†	95% confidence interval
	No.	%	No.	%		
Birth weight (g)						
<2,500	4	2.4	28	2.2	1.19	0.40, 3.56
2,500–3,999	116	70.7	974	77.5	1.00‡	
≥4,000	44	26.8	255	20.3	1.37	0.91, 2.06
Umbilical artery pH						
≥7.2	115	81.0	883	83.5	1.00‡	
<7.2	27	19.0	174	16.5	1.23	0.76, 1.99
Umbilical artery base deficit (mmol/liter)						
≥–12	138	100	1,012	98.2	1.00‡	
<–12	0		19	1.8	0.01	—§
Apgar score at 1 minute						
≥4	162	98.8	1,240	98.8	1.00‡	
<4	2	1.2	15	1.2	1.30	0.29, 5.76
Apgar score at 5 minutes						
≥4	164	100	1,251	99.7	1.00‡	
<4	0		4	0.3	0.05	—§
Neonatal intensive care						
No	147	89.6	1,113	88.3	1.00‡	
Yes	17	10.4	147	11.7	0.90	0.51, 1.58
Overall premature birth						
No	153	93.3	1,196	94.8	1.00‡	
Yes	11	6.7	65	5.2	1.19	0.59, 2.40
Spontaneous premature birth						
No	159	97.0	1,224	97.1	1.00‡	
Yes	5	3.0	37	2.9	0.93	0.32, 2.67
Small-for-gestational-age birth						
No	164	100	1,243	98.6	1.00‡	
Yes	0		18	1.4	0.01	—§
Respiratory distress						
No	160	97.6	1,225	97.1	1.00‡	
Yes	4	2.4	36	2.9	0.95	0.32, 2.78
Asphyxia						
No	162	98.8	1,251	99.2	1.00‡	
Yes	2	1.2	10	0.8	1.88	0.40, 8.76
Malformation						
No	163	99.4	1,238	98.2	1.00‡	
Yes	1	0.6	23	1.8	0.33	0.04, 2.53

* Data on the base deficit variable were missing for 256 newborns (18.0%), and data on the pH variable were missing for 226 newborns (15.9%). For the variables birth weight, neonatal intensive care, and Apgar score at 1 and 5 minutes, the prevalence of missing data was 0.1–0.4%.

† Odds ratios were adjusted for age, marital status, socioeconomic status, smoking habits, and body mass index.

‡ Referent.

§ Not calculated.

TABLE 4. Neonatal outcome according to the prevalence of antenatal anxiety disorder, Umeå University Hospital and Sunderby Central Hospital, Sweden, January 2000–January 2001

Variable	Antenatal anxiety disorder (exposed) (n = 64)*		No antenatal anxiety disorder (unexposed) (n = 1,261)*		Adjusted odds ratio†	95% confidence interval
	No.	%	No.	%		
Birth weight (g)						
<2,500	2	3.1	28	2.2	1.66	0.36, 7.75
2,500–3,999	48	75.0	974	77.5	1.00‡	
≥4,000	14	21.9	255	20.3	1.17	0.60, 2.27
Umbilical artery pH						
≥7.2	43	84.3	883	83.5	1.00‡	
<7.2	8	15.7	174	16.5	1.02	0.45, 2.28
Umbilical artery base deficit (mmol/liter)						
≥–12	50	98.0	1,012	98.2	1.00‡	
<–12	1	2.0	19	1.8	1.24	0.15, 10.25
Apgar score at 1 minute						
≥4	62	96.9	1,240	98.8	1.00‡	
<4	2	3.1	15	1.2	3.82	0.82, 17.82
Apgar score at 5 minutes						
≥4	64	100	1,251	99.7	1.00‡	
<4	0		4	0.3	0.06	—§
Neonatal intensive care						
No	58	90.6	1,113	88.3	1.00‡	
Yes	6	9.4	147	11.7	0.80	0.32, 1.99
Overall premature birth						
No	61	95.3	1,196	94.8	1.00‡	
Yes	3	4.7	65	5.2	1.02	0.30, 3.45
Spontaneous premature birth						
No	63	98.4	1,224	97.1	1.00‡	
Yes	1	1.6	37	2.9	0.61	0.08, 4.61
Small-for-gestational-age birth						
No	62	96.9	1,243	98.6	1.00‡	
Yes	2	3.1	18	1.4	1.32	0.26, 6.66
Respiratory distress						
No	64	100	1,225	97.1	1.00‡	
Yes	0		36	2.9	0.01	—§
Asphyxia						
No	63	98.4	1,251	99.2	1.00‡	
Yes	1	1.6	10	0.8	2.33	0.28, 19.27
Malformation						
No	64	100	1,238	98.2	1.00‡	
Yes	0		23	1.8	0.01	—§

* Data on the base deficit variable were missing for 243 newborns (18.3%), and data on the pH variable were missing for 217 newborns (16.4%). For the variables birth weight, neonatal intensive care, and Apgar score at 1 and 5 minutes, the prevalence of missing data was 0.1–0.5%.

† Odds ratios were adjusted for age, marital status, socioeconomic status, smoking habits, and body mass index.

‡ Referent.

§ Not calculated.

other potentially high-risk subgroups, such as smokers, women with a history of adverse neonatal/obstetric outcomes, and women with social vulnerabilities.

In line with our study results, Perkin et al. (27) did not find maternal anxiety and depression to be associated with obstetric complications such as preterm delivery, labor induction, labor acceleration, analgesia during the first stage of labor, and nonspontaneous delivery (all types of delivery other than spontaneous vaginal delivery) in a population of White women.

In our study, we found no association between depressive and/or anxiety disorders and preterm delivery or small-for-gestational-age birth. Because prevalence rates for preterm delivery are comparatively low in Sweden, our study only had enough statistical power to detect at least a doubling of the rate. However, given the fact that the rate of spontaneous preterm delivery was actually lower among women with any PRIME-MD diagnosis than among healthy subjects, it is unlikely that a larger sample size would have yielded different results. Nevertheless, it must be emphasized that our results might not be generalizable to other populations, particularly those with higher rates of preterm birth. Furthermore, in the unadjusted analysis, a borderline-significant association between antenatal depression and a birth weight of 4,000 g or more was evident. This association was lost in the multivariate analysis, probably because of the adjustment for maternal body mass index. Adjustment was also made for smoking, which is known to deteriorate fetal growth. A reasonable explanation for the absent associations between depressive disorders and deteriorated birth weight in the adjusted analyses might be that obesity and smoking have opposite effects on fetal growth. Although this was not assessable within the study design, this suggestion implies that the diagnosis of intrauterine growth restriction, particularly among obese depressed subjects, might be beyond our screening interventions, since a number of growth-restricted fetuses would be found within the normal range for fetal growth.

Given these limitations to the interpretation of our results, our study indicates that in otherwise healthy populations with well-established antenatal care, depressive and/or anxiety disorders per se appear not to affect the risk of preterm birth, low birth weight, and/or small-for-gestational-age birth. Apart from the assessment of clinical diagnoses and the population-based sample, yet another strength of our study was that second-trimester ultrasound screening was used for estimation of gestational length, leaving no doubt as to whether or not gestational age was correct (14).

A striking finding in prior studies is that use of psychopharmacologic medication often remains unclear. In our study, only two women were noted to use antidepressant medications during pregnancy. Although these figures might be due to the unwillingness of women to inform their midwife or obstetrician of the use of such drugs, the low frequency of psychoactive medication use could also be explained by cultural traditions, implying that women in Sweden and their physicians try, as far as possible, to avoid using medication during pregnancy and lactation. The matter of medication use might be of interest, since prior research has found associations between antidepressant therapy, a shorter duration of gestation, and lower birth weight (28, 29). Unfortunately, these studies investigated gestational age as a continuous variable and not preterm delivery as an outcome. A limitation of the present investigation is that the assessment of psychiatric diagnoses was made at only one time point during pregnancy, raising questions about whether symptoms remained unchanged, were transitory, or might have developed after the point of screening. For example, Evans et al. (30) noted a significant increase in depression scores between 18 and 32 weeks of pregnancy. Accordingly, Hoffman and Hatch (3) found that, independent of social class, depression scores were higher in the third trimester of pregnancy than in the first and second trimesters.

In conclusion, this study indicates that maternal antenatal depressive disorders and/or anxiety disorders are not independent risk factors for deteriorated neonatal outcome, such as preterm delivery and small-for-gestational-age birth, in a country with well-developed welfare systems. Further research is needed to explore associations with health care utilization during pregnancy, complications of delivery, and psychiatric health postpartum. There is also a need for more research on possible long-term effects of such disorders on children's development.

ACKNOWLEDGMENTS

This study was supported by research grants from Pfizer AB (Stockholm, Sweden), Visare Norr (Umeå, Sweden), and Umeå University Insamlingsstiftelsen (Umeå, Sweden) and by grants to Dr. Inger Sundström-Poromaa from the Swedish Society for Medical Research (Stockholm, Sweden).

The authors thank all personnel involved in ultrasound screening at the two study sites. The authors are especially grateful to Marie Wallgren and Yvonne Hoff, who provided invaluable help with the telephone interviews.

REFERENCES

1. Orr ST, James SA, Blackmore Prince C. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. Am J Epidemiol 2002;156:797–802.
2. Chung TK, Lau TK, Yip AS, et al. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosom Med 2001;63:830–4.
3. Hoffman S, Hatch MC. Depressive symptomatology during pregnancy: evidence for an association with decreased fetal growth in pregnancies of lower social class women. Health Psychol 2000;19:535–43.
4. Sjostrom K, Thelin T, Valentin L, et al. Do pre-, early, and mid-pregnancy life events influence gestational length? J Psychosom Obstet Gynecol 1999;20:170–6.
5. Dole N, Savitz DA, Hertz-Picciotto I, et al. Maternal stress and preterm birth. Am J Epidemiol 2003;157:14–24.
6. Hobel CJ, Dunkel-Schetter C, Roesch SC, et al. Maternal plasma corticotropin-releasing hormone associated with stress at 20 weeks of gestation in pregnancies ending in preterm deliv-

ery. Am J Obstet Gynecol 1999;180:S257–63.
7. Ellis MJ, Livesey JH, Inder WJ, et al. Plasma corticotropin-releasing hormone and unconjugated estriol in human pregnancy: gestational patterns and ability to predict preterm delivery. Am J Obstet Gynecol 2002;186:94–9.
8. McGrath S, McLean M, Smith D, et al. Maternal plasma corticotropin-releasing hormone trajectories vary depending on the cause of preterm delivery. Am J Obstet Gynecol 2002;186:257–60.
9. Hedegaard M, Henriksen TB, Sabroe S, et al. The relationship between psychological distress during pregnancy and birth weight for gestational age. Acta Obstet Gynecol Scand 1996;75:32–9.
10. Jacobsen G, Schei B, Hoffman HJ. Psychosocial factors and small-for-gestational-age infants among parous Scandinavian women. Acta Obstet Gynecol Scand Suppl 1997;165:14–18.
11. Piyasil V. Anxiety and depression in teenage mothers: a comparative study. J Med Assoc Thai 1998;81:125–9.
12. Miranda J, Azocar F, Komaromy M, et al. Unmet mental health needs of women in public-sector gynecologic clinics. Am J Obstet Gynecol 1998;178:212–17.
13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition: DSM-IV. Washington, DC: American Psychiatric Association, 1994.
14. Swedish Council on Technology Assessment in Health Care. Reports from the Swedish Council on Technology Assessment in Health Care (SBU). Int J Technol Assess Health Care 1999;15:424–36.
15. Spitzer RL, Williams JB, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care: The PRIME-MD 1000 Study. JAMA 1994;272:1749–56.
16. Lepine JP, Gastpar M, Mendlewicz J, et al. Depression in the community: the first pan-European study DEPRES (Depression Research in European Society). Int Clin Psychopharmacol 1997;12:19–29.
17. Blondel B, Kaminski M. Trends in the occurrence, determinants, and consequences of multiple births. Semin Perinatol 2002;26:239–49.
18. Andersson L, Sundstrom-Poromaa I, Bixo M, et al. Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. Am J Obstet Gynecol 2003;189:148–54.
19. Blackmore CA, Savitz DA, Edwards LJ, et al. Racial differences in the patterns of preterm delivery in central North Carolina, USA. Paediatr Perinat Epidemiol 1995;9:281–95.
20. Berkowitz GS, Blackmore-Prince C, Lapinski RH, et al. Risk factors for preterm birth subtypes. Epidemiology 1998;9:279–85.
21. Hamilton BE, Martin JA, Sutton PD. Births: preliminary data for 2002. Natl Vital Stat Rep 2003;51:1–20.
22. Diket AL, Nolan TE. Anxiety and depression: diagnosis and treatment during pregnancy. Obstet Gynecol Clin North Am 1997;24:535–58.
23. Blackmore CA, Ferre CD, Rowley DL, et al. Is race a risk factor or a risk marker for preterm delivery? Ethn Dis 1993;3:372–7.
24. Blackmore-Prince C, Kieke B Jr, Kugaraj KA, et al. Racial differences in the patterns of singleton preterm delivery in the 1988 National Maternal and Infant Health Survey. Matern Child Health J 1999;3:189–97.
25. Kelly RH, Russo J, Holt VL, et al. Psychiatric and substance use disorders as risk factors for low birth weight and preterm delivery. Obstet Gynecol 2002;100:297–304.
26. Hedegaard M, Henriksen TB, Secher NJ, et al. Do stressful life events affect duration of gestation and risk of preterm delivery? Epidemiology 1996;7:339–45.
27. Perkin MR, Bland JM, Peacock JL, et al. The effect of anxiety and depression during pregnancy on obstetric complications. Br J Obstet Gynecol 1993;100:629–34.
28. Ericson A, Kallen B, Wiholm B. Delivery outcome after the use of antidepressants in early pregnancy. Eur J Clin Pharmacol 1999;55:503–8.
29. Simon GE, Cunningham ML, Davis RL. Outcomes of prenatal antidepressant exposure. Am J Psychiatry 2002;159:2055–61.
30. Evans J, Heron J, Francomb H, et al. Cohort study of depressed mood during pregnancy and after childbirth. BMJ 2001;323:257–60.