

Depressive Symptoms in Mothers of Infants Identified as Genetically at Risk for Type 1 Diabetes

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OBJECTIVE— This study describes maternal depression associated with newborn genetic screening for type 1 diabetes after risk notification.

RESEARCH DESIGN AND METHODS— Mothers of at-risk infants ($n = 192$), identified through newborn genetic screening as part of the Prospective Assessment of Newborns for Diabetes Autoimmunity study, were administered a structured telephone interview assessing maternal depressive symptoms 1 and 3.5 months after risk notification. Statistical analyses were conducted to examine predictors and correlates of maternal depressive symptoms.

RESULTS— For the total sample, maternal depressive symptoms in response to infant risk status were not elevated at 1 and 3.5 months after risk notification. However, at the first interview, mothers from ethnic minority backgrounds ($P < 0.002$), with limited education ($P < 0.001$), and with postpartum depression symptomatology ($P < 0.001$) reported significantly more depressive symptoms in response to risk notification ($r^2 = 0.354$). At the second interview, postpartum depression symptomatology remained a powerful predictor of depressive symptoms in response to risk notification ($P < 0.001$). In addition, certain coping styles (wishful thinking, self-blame, and seeking social support) were associated with increased depressive symptoms. A history of major depression was a correlate of both postpartum depressive symptomatology ($r = 0.26$) and maternal depressive response to risk notification ($r = 0.21$).

CONCLUSIONS— For the most part, mothers of infants genetically at risk for type 1 diabetes do not appear to evidence elevated depressive symptoms. This suggests that most mothers are resilient when notified of infant risk. However, certain maternal characteristics such as ethnic minority status, less than a high school education, postpartum depression symptomatology, a history of major depression, and certain coping strategies (wishful thinking, self-blame, and seeking social support) appear to be associated with a more difficult maternal response to the news of an infant's increased genetic risk for type 1 diabetes.

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Abbreviations: CES-D, Center for Epidemiologic Studies–Depression Scale; EPDS, Edinburgh Postnatal Depression Scale; NMIHS, National Maternal and Infant Health Survey; PANDA, Prospective Assessment of Newborns for Diabetes Autoimmunity; SCID, Structured Clinical Interview for DSM-IV Axis I Disorders; WCC, Ways of Coping Checklist.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Predictive genetic testing is now available for 1,000 diseases including type 1 diabetes (1). The goal of predictive genetic testing is either to provide early intervention, to delay disease onset, or to prevent a disease in at-risk individuals (2). However, our ability to prevent a disease lags behind our ability to identify those genetically at risk. Some argue that the "genetic window" has been opened without full consideration of the impact of disease risk identification in the absence of effective treatment or prevention (3,4). This current environment raises a need to fully elucidate the ways individuals and family members respond psychologically to the news of increased genetic risk for a disease that cannot be prevented (5–7).

Advances in genetic research have identified the HLA region of chromosome 6 as controlling the immune response and susceptibility to type 1 diabetes (8,9). Newborn genetic screening programs for type 1 diabetes are now available worldwide, although there is no known method to prevent the disease (2). Few studies have examined the psychological impact of informing a parent of a child's increased risk for type 1 diabetes. These studies suggest that risk notification is not associated with excessively high levels of anxiety or parenting stress, although a variety of factors are associated with parental response, such as education, ethnic minority status, risk perception accuracy, and the child's actual risk for type 1 diabetes (10,11).

Prior studies have not examined maternal depressive symptoms in response to the news that a child is at increased risk for type 1 diabetes. Depression is common in women (lifetime prevalence of ~21%), and women appear to be particularly vulnerable postpartum, with 10–15% of women reporting the "baby blues" (12–14). The aim of this study was to examine the level of maternal depressive symptoms in response to the news that a child is genetically at risk for type 1 dia-

Table 1—Participant characteristics

Characteristic	
Maternal characteristics	
Age at risk notification (years)	28.21 ± 6.00
Maternal ethnicity	
Caucasian	150 (78.1)
African American	27 (14.1)
Hispanic American	8 (4.2)
Asian American	2 (1.0)
Did not report	5 (2.6)
Marital status	
Married	136 (70.8)
Never married	48 (25.0)
Divorced/separated	7 (3.6)
Did not report	1 (0.6)
Maternal education	
Some high school	26 (13.5)
Graduated high school	43 (22.4)
Some college	61 (31.8)
Graduated college	42 (21.9)
Some graduate school	2 (1.0)
Completed graduate school	18 (9.4)
Child characteristics	
Age at risk notification (days)	308.93 ± 163.22
Risk status	
Moderate	136 (70.8)
High	55 (28.6)
Extremely high	1 (0.6)
Number of children in household	
1	68 (35.4)
2	72 (37.5)
≥3	51 (26.6)
Did not report	1 (0.6)
Family history of diabetes	
No family history	67 (34.9)
First-degree relative	14 (7.3)
Second-degree relative	111 (57.8)

Data are n (%) or means ± SD.

betes. We hypothesized that mothers with a history of major depression or postpartum depression symptomatology would evidence increased depressive symptoms 1 and 3.5 months after risk notification. A number of additional potential predictors of maternal response such as educational level, ethnic minority status, and coping style were also examined.

RESEARCH DESIGN AND METHODS

Mothers were recruited from the Prospective Assessment of Newborns for Diabetes Autoimmunity (PANDA) study, funded by the National Institutes of Health and the Juvenile Diabetes Research Foundation, to identify newborns at risk for type 1 diabetes through genetic testing (15). Mothers in this study had been recruited from three Florida cities (Gainesville, Panama City, and Orlando). Shortly after a child's birth, mothers provided informed consent, and blood samples obtained for state-mandated newborn metabolic screening were used. Mothers were told they would be recontacted only if their child was at increased risk for type 1 diabetes.

Based on the child's HLA-DQB1 allele status and family history of diabetes, infants were assigned to one of six risk categories: protected, very low, low, moderate, high, and extremely high (16). Mothers of children in the protected, very low, and low risk categories were not recontacted. Mothers of infants in the moderate, high, and extremely high risk categories were contacted by telephone and provided information about the infant's risk status using a standardized script. Mothers were given both the label describing the risk category as well as a numerical estimate: moderate risk (2 of 100 babies), high risk (5–10 of 100 babies), and extremely high risk (20–25 of 100 babies). Mothers were told that the infant's increased risk did not mean the child would definitely develop diabetes. Questions were answered, and each mother was asked permission to be contacted by our research team for a follow-up telephone interview.

In the current study, 212 mothers were contacted, and 192 mothers (90.6%) agreed to the telephone interview. Table 1 displays the demographic characteristics of the sample. Most mothers were Caucasian, married, and college-educated and had newborns in the moderate-risk category.

A structured telephone interview was conducted with the 192 mothers who agreed to participate 1 month (28.6 ± 22.9 days) after risk notification. Mothers were recontacted 2.5 months later (78.6 ± 20.2 days). Thirteen mothers declined the second interview, and we were unable to reach 35 mothers, resulting in a second interview sample of 144 (75%).

The 20-item Center for Epidemio-

logic Studies–Depression Scale (CES-D) (17) was used to assess depressive symptoms in response to risk notification. Large-sample normative data and clinical cutoff scores (≥16) are available (17,18). Mothers were asked to respond to each CES-D item while thinking specifically about the newborn's risk for type 1 diabetes. The CES-D was included in both the first and second interviews. The measure demonstrated excellent internal consistency (first interview, $\alpha = 0.92$; second interview, $\alpha = 0.90$).

Predictors of depressive symptoms

During the first interview, the Past Major Depressive Disorder section of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID) (19) was used to determine whether the mother had a history of major depression. The SCID is a commonly used psychiatric assessment tool with good psychometric properties (20–23). In analyses predicting to CES-D scores, mothers who had a history of major depression were coded as 1; all others were coded 0.

The 10-item Edinburgh Postnatal Depression Scale (EPDS) (24) was administered during the first interview. Clinical cutoff scores (≥13) and large-sample normative data are available (25). The measure demonstrated excellent internal consistency in the current sample ($\alpha = 0.89$). In analyses predicting CES-D scores, mothers who scored at or above the clinical cutoff were coded as 1; all others were coded 0.

A modified version of the Ways of Coping Checklist (WCC) (26) was used to assess how mothers coped with the news of the child's increased risk for type 1 diabetes. The WCC was administered at the second interview only. Mothers were asked to think about how they had coped with the news of the child's increased diabetes risk over the last few months. Items describing different coping strategies were read to the mother, and she indicated whether or not she had used that strategy. The percentage of affirmative responses to items comprising five different coping scales was calculated, yielding five coping scores: problem-focused ($\alpha = 0.85$), seeks social support ($\alpha = 0.78$), wishful thinking ($\alpha = 0.82$), avoidance ($\alpha = 0.65$), and blamed self ($\alpha = 0.82$).

Maternal characteristics tested for association with maternal depressive symptoms (CES-D) included: maternal age,

Table 2—Predictors of maternal depressive symptoms in response to risk notification

Variable	n	B ± SE	b	P	r ²
First interview CES-D	192				0.354
Ethnic minority status		4.19 ± 1.29	0.19	0.001	
Maternal education		-1.61 ± 0.39	-0.25	<0.001	
Postpartum depression		0.68 ± 0.09	0.45	<0.001	
Second interview CES-D	144				0.484
First Interview CES-D		0.14 ± 0.06	0.15	0.033	
Postpartum depression		0.41 ± 0.09	0.32	<0.001	
Seeks social support coping		0.03 ± 0.01	0.16	0.012	
Wishful thinking coping		0.04 ± 0.02	0.15	0.039	
Self-blaming coping		0.15 ± 0.03	0.32	<0.001	

Ethnic minority status coded 1 for African American, Hispanic American, or Asian American and 0 for Caucasian. Maternal education coded 1 for some college and 0 for high school or less. Postpartum depression coded 1 for ≥13 (clinical cutoff) on the EPDS and 0 for <13.

ethnic minority status (coded 1 = African American, Hispanic American, Asian American, 0 = Caucasian), education (coded 1 = some college, 0 = high school), marital status (1 = never married, divorced, or separated, 0 = married), and family income (1 = ≤\$10,000 to 11 = ≥\$100,000). Child variables included: child age at the time of risk notification, child sex, risk status (1 = high and extremely high risk, 0 = moderate risk), first-degree relative with diabetes (1 = yes, 0 = no), at least one second-degree relative with diabetes (1 = yes, 0 = no), mother's first child (1 = yes, 0 = no), and number of children in the household.

Because prior studies have found that time since risk notification is predictive of maternal anxiety and accuracy of risk perception (11,16), this variable was also tested as a predictor of maternal depressive symptoms (CES-D) at both the first and second interviews.

Statistical analysis

Statistical analysis was performed using SPSS Version 13. Welch's *t* tests were used to compare maternal CES-D scores with the CES-D normative sample of 2,514 individuals (9.25 ± 8.58) (17) and with data from 7,600 mothers assessed 17 months after childbirth as part of the 1988 National Maternal and Infant Health Survey (NMIHS) (10.3 ± 10.1) (18). Comparison of the first and second interview CES-D scores was performed using a paired-samples *t* test. Association among the measures of depression was conducted with Pearson correlational analysis.

Hierarchical linear regression was

used to identify predictors of first and second interview CES-D scores. Variables were entered in predetermined blocks: time since risk notification, maternal characteristics, child characteristics, history of major depression, evidence of postpartum depression symptomatology, and WCC coping styles. Controlling for time since risk notification, the order of variable entry was determined by the entry of more general maternal and child characteristics first, followed by characteristics presumed to be more specifically associated with the mother's reaction to the genetic test results such as her history of major depression, her report of postpartum depression symptomatology, and how she coped with the news of her infant's increased risk. After each block of variables was entered, variables that failed to exhibit predictive power (*P* > 0.15) were dropped from further consideration. In the final model, only variables that exhibited significant predictive power (*P* < 0.05) were retained. When the second interview CES-D scores were predicted, the first interview CES-D score was entered first, followed by the same order of entry for blocks of variables used to predict first interview CES-D scores.

Using a similar approach of variable entry, logistic regression was used to compare the characteristics of mothers who completed the first interview only and those mothers who completed both interviews.

RESULTS— Because all three measures of depression used in this study have published clinical cutoff scores, the percentage of women above the clinical

cutoff was calculated: 11.5% on the CES-D, 12.5% on the EPDS, and 18.2% on the SCID. These rates are all consistent with published population estimates (12–14,17,18). The percentage of women above the clinical cutoff on the CES-D actually declined at the time of the second interview to 7.6%.

First interview: depressive symptoms in response to risk notification

At the time of the first interview, mothers' CES-D scores (6.30 ± 8.65) were significantly lower than the CES-D normative sample scores (17) [Welch's *t*(220) = 4.56, *P* < 0.001] and scores obtained from the NMIHS postpartum sample (18) [Welch's *t*(204) = 6.30, *P* < 0.001].

Although CES-D scores were not elevated for the group as a whole, there was considerable variability in responses. Results of the hierarchical multiple regression analysis are displayed in Table 2. Ethnic minority status, education, and evidence of postpartum depression symptomatology were all significant predictors of CES-D scores. Ethnic minority mothers had higher CES-D scores (10.34 ± 10.72) than Caucasian mothers (5.32 ± 7.87). Mothers with high school education or less reported higher scores (9.62 ± 10.28) than mothers with some college education (4.44 ± 6.97). Mothers who scored above the clinical cutoff on the EPDS exhibited very elevated CES-D scores (15.21 ± 14.56) compared with those who were below the EPDS clinical cutoff (5.03 ± 6.59).

Second interview: depressive symptoms in response to risk notification

Although CES-D scores obtained at the second interview were slightly lower than those obtained at the first interview, the difference was not statistically significant.

Results of the hierarchical multiple regression analysis indicated that first interview CES-D scores, evidence of postpartum depression symptomatology, and coping style all predicted CES-D scores at the second interview (Table 2). Elevated CES-D scores at the first interview were associated with higher CES-D scores at the second interview (*r* = 0.45). Mothers who were above the clinical cutoff on the EPDS at the first interview continued to have extremely elevated CES-D scores at the time of the second interview (15.58 ± 15.00) compared with mothers below the

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EPDS clinical cutoff (3.84 ± 4.96). Greater use of seeks social support, wishful thinking, and blamed self coping strategies were all associated with elevated CES-D scores at the second interview.

Of note, a history of major depression was significantly associated with higher CES-D scores at the second interview until the EPDS score was entered in the regression analysis. The SCID score correlated with both the EPDS score ($r = 0.26, P < 0.01$) and the CES-D second interview score ($r = 0.21, P < 0.05$). However, the EPDS score correlated higher with the second interview CES-D score ($r = 0.50, P < 0.01$), and when it was entered into the regression with the SCID score, the SCID score was no longer significant. This suggests a possible mediational effect of symptoms of postpartum depression. Mothers with a history of major depression are more likely to experience postpartum depression symptomatology. Mothers who experience symptoms of postpartum depression are, in turn, more likely to respond with depressive symptoms to the news that the infant is at increased risk for type 1 diabetes.

Comparison of mothers who did and did not complete two interviews

We were able to complete second interviews for 75% of our sample; we were unable to reach 35 mothers, and 13 mothers declined the second interview. Using logistic regression, we examined differences between mothers who completed both interviews ($n = 144$) and those who did not ($n = 48$). Both ethnic minority status ($B = 0.83, P < 0.03$) and EPDS scores ($B = 0.05, P < 0.06$) proved to be predictors. Ethnic minority mothers were more common in the one-interview (31%) than the two-interview (17%) group. There were more mothers with scores above the EPDS cutoff in the one-interview (24%) versus two-interview group (10%).

CONCLUSIONS— Results from this sample of mothers in the PANDA study suggest that newborn genetic screening for type 1 diabetes risk does not lead to elevated depressive symptoms in most mothers. In fact, when asked to respond to infant risk for diabetes, mothers' scores on the CES-D were actually lower than previously reported in large normative samples, attesting to the resiliency of the participants. However, there was considerable variability in maternal responses.

Those from ethnic minority backgrounds and with limited education reported significantly more depressive symptoms at the first interview. A previous study documented high levels of anxiety in these subgroups as well (11). However, there is some evidence that ethnic minority women generally report more depressive symptoms than Caucasian women (27). Consequently, it is difficult to determine whether their higher CES-D scores are a product of this general trend or a specific response to the news of the child's increased diabetes risk. Future studies that examine ethnic minority versus majority maternal responses to both high-risk and low-risk genetic test results may help clarify these results.

Evidence of postpartum depression symptomatology was a particularly powerful predictor of depressive symptoms in response to risk notification. Postpartum depression is common, affecting about 10–15% of women. In this sample, 12.5% of mothers were above the clinical cutoff on the EPDS; a finding consistent with the 13% prevalence reported by O'Hara and Swain in their meta-analysis (13). Mothers who report symptoms of postpartum depression are very likely to respond to the news of the child's increased diabetes risk with high rates of depressive symptoms. These findings suggest that screening for postpartum depression symptomatology may help identify those mothers who may be particularly vulnerable to the news of a child's increased diabetes risk.

A history of major depression was also associated with higher levels of depressive symptoms in response to risk notification. However, when SCID and EPDS scores were considered in the same predictive model, the EPDS was the better predictor of depressive symptoms response. Correlational analyses suggested that postpartum depression symptomatology may mediate the relationship between a history of major depression and the extent of depressive response to the news of the child's increased risk for type 1 diabetes. It appears that a history of major depression increases a woman's risk for elevated symptoms of postpartum depression, which in turn increases the likelihood of a depressive response to risk notification.

Ethnic minority status and postpartum depression symptomatology were also important predictors of who com-

pleted two interviews or stayed in this interview study over time. Whether these maternal characteristics predict who stays in longitudinal natural history studies such as PANDA remains to be seen. However, these findings suggest that certain populations may find the challenges of long-term natural history studies more difficult than others.

The mother's preferred coping styles were also important predictors of depressive symptoms in response to risk notification. Frequent use of wishful thinking and blamed self coping strategies predicted higher levels of maternal depressive symptoms. These findings are consistent with a large body of literature suggesting that these coping styles are associated with poorer adaptation in response to stress (28). Unexpected was the association between seeks social support and higher depressive symptom reported on the CES-D, given that social support is often a buffer for depression (27). Seeking the support of others may have different ramifications in the context of newborn genetic screening, compared with other types of stress. Over two-thirds of this study's infants had a family history of diabetes. In these families, talking to others about the child's increased risk may have only escalated the mothers' concerns. Even in families with no history of diabetes, talking with others may increase maternal exposure to a whole host of fears, concerns, and misinformation shared by the general population. In this study, coping was assessed only at the second interview using a retrospective approach; the mother was asked to reflect on how she had coped with her child's increased diabetes risk over the last few months. It is certainly possible that the association seen between her coping responses and her second-interview CES-D scores are the product, rather than predictors, of the mother's depressive symptoms. Additional longitudinal studies will be needed to clarify the causal direction of the coping-depressive symptom associations reported here.

This study's findings are limited by characteristics of the PANDA sample studied. The PANDA study only follows newborns determined to be genetically at risk. Consequently, comparisons with mothers of newborns determined to be at low risk or protected were not possible. However, it seems likely that mothers informed that their infants were low risk or

protected would be relieved by such news, exhibiting even lower rates of depressive symptoms than those exhibited by the study samples. For this reason, the CES-D (17) and NMIHS (18) large normative sample data provide reasonable sources for comparison. Most of the PANDA study newborns had some family history of diabetes. Consequently, the extent to which the findings are replicated in the general population with no family history of this disease remains to be seen. Differential drop out of mothers from the first to the second interview may have limited our ability to detect significant ethnic minority effects at the second interview. Although more women with postpartum depression symptomatology failed to complete the second interview, postpartum depression remained a significant predictor of CES-D scores at the second interview. However, the differential loss of women experiencing postpartum depression symptomatology across interviews may have resulted in an underestimation of the power of this effect.

Although this and previous studies (10,11) suggest that most mothers do not appear to exhibit clinically significant levels of depression or anxiety in response to increased infant risk for type 1 diabetes, this research has been limited in focus and duration. We have yet to discern the longer-term impact of such studies on a variety of psychological and behavioral variables, such as maternal self-esteem and parenting style.

Newborn genetic screening programs for type 1 diabetes identify at-risk infants to be followed in natural history studies in which the pathogenesis of the disease can be documented, and potential interventions to prevent the disease can be identified. These studies cannot succeed unless the families of these at-risk infants remain committed to the research protocol for long periods of time. Although most mothers appear to be resilient in response to an infant's increased genetic risk, some may have a more difficult response. Understanding family members' response to risk notification and identifying those in need of additional psychological resources appear key to the success of these important studies.

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