Evolution of Depression and Anxiety Symptoms in Parents of Very Preterm Infants During the Newborn Period

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IMPORTANCE Mothers experience heightened depression and anxiety following very preterm (VPT) birth, but how these symptoms evolve during the first months after birth is unknown. Research on the psychological adjustment of fathers following VPT birth is limited.

OBJECTIVES To describe the trajectory and predictors of distress in parents of VPT infants during the first 12 weeks after birth, and to compare rates of depression and anxiety in parents of VPT infants with those in parents of healthy full-term (FT) infants shortly after birth and at 6 months' postnatal age.

DESIGN, SETTING, AND PARTICIPANTS Longitudinal, prospective, follow-up cohort study of depression and anxiety symptoms in parents of VPT infants (<30 weeks' gestational age; admitted to the neonatal intensive care unit at the Royal Women's Hospital, Melbourne, Australia, between January 21, 2011, and December 23, 2013), documented every 2 weeks until age 12 weeks and at age 6 months, as well as in parents of healthy FT infants (≥37 weeks' gestational age; birth weight >2499 g; born at the Royal Women's Hospital between August 15, 2012, and March 26, 2014; not admitted to the neonatal nursery) shortly after birth and at age 6 months.

EXPOSURE Birth of a VPT infant.

MAIN OUTCOMES AND MEASURES Symptoms of depression (Center for Epidemiological Studies Depression Scale) and anxiety (Hospital Anxiety and Depression Scale).

RESULTS The study included 113 mothers (mean [SD] age at birth, 32.7 [5.3] years) and 101 fathers (mean [SD] age at birth, 34.7 [6.4] years) of 149 VPT infants (49% male; 84 singletons, 65 multiples; mean [SD] birth weight, 1021 [261] g) as well as 117 mothers (mean [SD] age at birth, 32.9 [4.8] years) and 110 fathers (mean [SD] age at birth, 35.9 [5.3] years) of 151 healthy FT infants (50% male; 149 singletons, 2 multiples; mean [SD] birth weight, 3503 [438] g). Mean scores and rates of depression and anxiety reduced over time for parents of VPT infants in the 12 weeks after birth: the mean (95% CI) change in depression score per week was −0.52 (−0.73 to −0.31; P < .001) for mothers and −0.39 (−0.56 to −0.21; P < .001) for fathers; the mean (95% CI) change in anxiety score per week was −0.16 (−0.26 to −0.06; P = .003) for mothers and −0.22 (−0.31 to −0.15; P < .001) for fathers. However, rates never dropped below 20%. Few perinatal or social risk factors predicted longitudinal changes in depression or anxiety. Compared with parents of FT infants, parents of VPT infants had higher rates of depression shortly after birth (mothers: 6% vs 40%; odds ratio [OR] = 9.9; 95% CI, 4.3 to 23.3; P < .001; fathers: 5% vs 36%; OR = 11.0; 95% CI, 4.1 to 29.6; P < .001) and at 6 months (mothers: 5% vs 14%; OR = 2.9; 95% CI, 1.0 to 8.2; P = .04; fathers: 6% vs 19%; OR = 3.4; 95% CI, 1.3 to 9.0; P = .01) as well as anxiety shortly after birth (mothers: 13% vs 48%; OR = 6.5; 95% CI, 3.3 to 12.6; P < .001; fathers: 10% vs 47%; OR = 7.8; 95% CI, 3.7 to 16.8; P < .001) and at 6 months (mothers: 14% vs 25%; OR = 2.1; 95% CI, 1.0 to 4.3; P = .05; fathers: 10% vs 20%; OR = 2.3; 95% CI, 1.0 to 5.3; P = .05).

CONCLUSIONS AND RELEVANCE Mothers and fathers of VPT infants had elevated rates of depression and anxiety symptoms that declined over time, although remaining above expected levels throughout the newborn period and at 6 months.

Published online July 18, 2016.

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Understanding mental health in parents of very preterm (VPT) infants is critical as parental depression and anxiety can adversely affect children’s development. While more mothers of preterm infants experience psychological distress in the early years than mothers of infants born at full term (FT), there is a dearth of detailed, longitudinal information on these symptoms in the newborn period. In the first hours and days after birth, fathers are faced with the dual responsibility of caring for their partners after delivery and being the primary point of contact with their child. Most remain involved in the day-to-day care of their infants throughout their hospital stay, often juggling responsibilities while returning to the workforce. However, research to date has largely overlooked fathers.

The newborn period is stressful for parents following VPT birth. Small studies of parents of very low-birth-weight infants during the newborn period have shown that 30% to 50% of mothers and 30% to 60% of fathers experienced clinically significant symptoms of depression. Longitudinal studies are limited, but most report sustained symptoms in the first year after VPT birth. Singer et al assessed symptoms of psychological distress in mothers of very low-birth-weight infants from shortly after birth until 36 months’ corrected age. They found initially higher rates of psychological distress compared with mothers of FT infants that generally declined over time. However, to our knowledge, no previous study has examined how distress changes during the critical period in which the infant is hospitalized. Although there is less research on parental anxiety than depression shortly after VPT birth, around 25% of mothers and 15% of fathers experience elevated anxiety just after neonatal intensive care unit (NICU) discharge.

It is unclear which parents of VPT infants are at higher risk for depression and anxiety. Findings regarding medical risk factors for parental mental health difficulties following VPT birth are mixed, and few studies have examined the effects of these risk factors over time. Bronchopulmonary dysplasia has been associated with higher depression scores in mothers of very low-birth-weight infants and a slower decline in symptom severity during the first 3 years. Similarly, it was reported that parental anxiety severity is associated with neonatal medical factors. In contrast, other studies reported that medical risk factors were not associated with increased psychological distress. We could find no studies examining the effects of medical risk factors on the evolution of distress during the very early period following VPT birth.

This study addressed gaps in the literature by repeatedly assessing depression and anxiety in mothers and fathers of VPT infants throughout the newborn period. We aimed to (1) describe the trajectory of depression and anxiety symptoms during the first 12 weeks after birth in parents of VPT infants, (2) examine the influence of social and perinatal characteristics on these trajectories, and (3) compare symptoms of depression and anxiety shortly after birth and at 6 months’ postnatal age in parents of VPT and FT infants.

Methods

Sample

Families with VPT infants (<30 weeks’ gestational age) admitted to the NICU between January 21, 2011, and December 23, 2013, at the Royal Women’s Hospital, Melbourne, Australia, were eligible. The comparison group comprised families of healthy FT infants born at 37 weeks’ gestational age or later with a birth weight greater than 2499 g at the Royal Women’s Hospital between August 15, 2012, and March 26, 2014, and not admitted to the neonatal nursery. Parents who did not speak English and infants who had congenital abnormalities likely to influence development or were considered unlikely to survive according to the attending medical team were excluded. The data analysis was conducted between January 2015 and February 2016.

Families of 291 eligible VPT infants were approached to take part in the study, with those of 150 infants (52%) agreeing to participate (including 31 sets of twins and 1 set of triplets). One infant was subsequently excluded from the study owing to a congenital abnormality, leaving 149 infants from 116 families. Parental mental health data were collected from a total of 113 mothers and 101 fathers. Six infants died while in the hospital. Data from these parents until the time the child died were used, with the exception of 1 family whose infant died prior to any questionnaires being completed. Complete data were also used for 2 families who had a surviving twin.

Families of 294 eligible FT infants were approached, and those of 151 infants (51%) agreed to participate. The FT sample comprised 149 singletons and 1 set of twins, with 117 mothers and 110 fathers from the FT group providing mental health data.

Procedure

The research protocol was approved by the Royal Women's Hospital Human Research Ethics Committee. After written informed consent was obtained, parents of VPT infants were asked to complete standardized self-report questionnaires measuring depression and anxiety symptoms every 2 weeks from recruitment (shortly after birth) until the infant reached term-equivalent age (40 weeks’ postmenstrual age) and again.
6 months after birth. Parents of FT infants completed the measure once within 3 weeks of birth and at 6 months. When a parent scored above clinical thresholds on any of the mental health questionnaires, a member of the research team contacted him or her to discuss the scores. The families of all VPT infants were offered support services (including social work and mental health support) routinely throughout their admission.

**Measures**

Symptoms of depression were assessed with the Center for Epidemiological Studies Depression Scale (CES-D).13 The CES-D is a widely used and validated screening tool for depression and has been used with parents of VPT infants.14,15 A score of 16 or higher on the CES-D represents clinically significant depressive symptoms.

The anxiety scale from the Hospital Anxiety and Depression Scale16 assessed symptoms of anxiety. A score of 8 or higher was used to indicate possible anxiety.17 The Hospital Anxiety and Depression Scale has been validated and performs well in screening for anxiety disorders,18 including in parents of preterm infants.19

Primary caregivers completed the Social Risk Index, a composite score based on 6 items: family structure, education of primary caregiver, occupation of primary income earner, employment status of primary income earner, language spoken at home, and maternal age at birth.20 Families were categorized around the median score of 1 as higher (>1) or lower (0 or 1) social risk.20,21 Additional information gathered from parents included number of other children as well as access to NICU support services and mental health services in the previous year.

Research nurses collected maternal and perinatal data from the infants’ medical histories (Table 1), dates of transfer to other hospitals, and dates of discharge home.

### Statistical Analysis

The level and prevalence of depression and anxiety in mothers and fathers of VPT infants at 2, 4, 6, 8, 10, and 12 weeks after birth were described using the mean and standard deviation for continuous outcomes and using the proportion of parents scoring above clinical cutoff scores. The score at each time point was taken from the questionnaire completed within ±7 days of the fortnightly time points. Twelve weeks was chosen as the upper limit for this analysis as beyond this time there were fewer parental responses and the data became less representative; only parents of infants born at less than 28 weeks’ gestational age were given questionnaires beyond 12 weeks.

Changes over time during the newborn period in depression and anxiety in parents of VPT infants only were described using mixed-effects linear regression models fitted to the repeated measures of the continuous score on each questionnaire (CES-D and Hospital Anxiety and Depression Scale) at the family level. Chronological age was used as the timescale in the regression model, and models were fitted using a random intercept and random slope (effect of time) to allow for the repeated observations within an individual. All analyses were performed separately for mothers and fathers.

A time-dependent covariate (prior to 7 days, within 7 days, and after 7 days of discharge or transfer) was added to the mixed models to assess whether depression and anxiety symptoms varied around the time of discharge home or transfer between hospitals. Effect modification by perinatal and social predictors (social risk, access to mental health services in the 12 months prior, access to NICU support services, older siblings, assisted conception, plurality, gestational age, resuscitation at birth, and length of ventilation [proxy for overall illness severity]) was assessed by adding both the perinatal predictor and an interaction between the predictor and chronological age to the mixed-effects models. For infant-level factors, the perinatal characteristic of the sicker infant was used as the predictor in the case of multiples.

Measurements of depression and anxiety taken shortly after birth and at age 6 months were compared between parents of VPT and FT infants using linear and logistic regression for continuous and binary outcomes, respectively, adjusted for social risk, plurality, and siblings.
Statistical analyses were performed using Stata version 13.1 statistical software (StataCorp LP).

Results

Sample Characteristics
The study included 113 mothers (mean [SD] age at birth, 32.7 [5.3] years) and 101 fathers (mean [SD] age at birth, 34.7 [6.4] years) of 149 VPT infants (49% male; 84 singletons, 65 multiples; mean [SD] birth weight, 1021 [261] g) as well as 117 mothers (mean [SD] age at birth, 32.9 [4.8] years) and 110 fathers (mean [SD] age at birth, 35.9 [5.3] years) of 151 healthy FT infants (50% male; 149 singletons, 2 multiples; mean [SD] birth weight, 3503 [438] g). The proportion of male infants and the mean parental ages were similar between the VPT and FT groups, but the VPT group compared with the FT group had fewer singletons (56% vs 99%, respectively) and more families classified as higher social risk (55 of 128 [43%] vs 32 of 126 [25%], respectively). Bronchopulmonary dysplasia, grade III or IV intraventricular hemorrhage, and suspected or proven necrotizing enterocolitis occurred in a minority of the VPT group (31%, 3%, and 11%, respectively) (Table 1).

Trajectories of Depression and Anxiety Symptoms in Parents of VPT Infants

Symptoms of Depression
In both mothers and fathers, depression symptoms decreased during the first 12 weeks from birth (Figure 1A). The mean change in CES-D depression score per week was −0.52 (95% CI, −0.73 to −0.31; P < .001) for mothers and −0.39 (95% CI, −0.56 to −0.21; P < .001) for fathers.

The proportion of parents experiencing depression above the clinical cutoff score was initially high (40%) for both mothers and fathers. The rate of elevated depression symptoms decreased during the first 12 weeks from birth, with the exception of a slight increase at 12 weeks (Figure 1B). Throughout this period, the rate of mothers and fathers with elevated depression symptoms never dropped below 20%.

Symptoms of Anxiety
In both mothers and fathers, anxiety levels decreased during the first 12 weeks from birth, although a slight increase in maternal anxiety was observed at 12 weeks (Figure 2A). The mean change in anxiety score per week was −0.16 (95% CI, −0.26 to −0.05; P = .003) for mothers and −0.22 (95% CI, −0.31 to −0.15; P < .001) for fathers.

The proportions of both mothers and fathers with elevated anxiety symptoms was also initially high, approaching 50% for both. This rate again decreased over time with a slight increase in mothers at 12 weeks (Figure 2B). Throughout the newborn period, the rate of mothers with elevated anxiety symptoms never dropped below 22%, while for fathers the lowest rate was 25%.

Depression and Anxiety Levels Around the Time of Discharge and Transfer
There was some evidence that mothers were less anxious from 1 week after being transferred (anxiety score mean difference, −1.16; 95% CI, −2.22 to −0.10; P = .03) and possibly around the time of discharge (anxiety score mean difference, −0.64; 95% CI, −1.96 to 0.68; P = .34), compared with prior to transfer or discharge. The evidence for a decline in anxiety symptoms over time was lessened after adjustment for varied anxiety around the time of and after transfer and discharge (mean change in anxiety score per week, at transfer: −0.08; 95% CI, −0.20 to 0.05; P = .24;
at discharge: −0.11; 95% CI, −0.24 to 0.02; \(P = .09\) (eTable 1 in the Supplement). There was little evidence that anxiety in fathers varied around the time of discharge or transfer, with similar estimates of the change over time after adjustment for these variables.

There was little evidence that the level of depression in mothers or fathers varied around the time of or after discharge compared with more than 1 week prior to discharge, except possibly within 1 week of transfer for fathers (depression score mean difference, −1.90; 95% CI, −4.16 to 0.36; \(P = .10\)). Allowing for different levels of depression at these times had little effect on the estimate of the change over time.

Perinatal and Social Predictors of Depression and Anxiety in Parents of VPT Infants

Overall, there was little evidence that perinatal or social predictors moderated the changes of depression and anxiety scores over time since birth (eTable 2 in the Supplement). However, there was evidence that depression in mothers with previous children decreased more slowly over time than in mothers with no previous children (interaction, \(\beta = 0.46; 95\% \text{ CI}, 0.04 \text{ to } 0.87; P = .03\)). Also, both depression and anxiety decreased more quickly in fathers who accessed NICU support services during their stay (interaction, depression: \(\beta = −0.58; 95\% \text{ CI}, −1.04 \text{ to } −0.12; P = .01\); anxiety: \(\beta = −0.30; 95\% \text{ CI}, −0.51 \text{ to } −0.10; P = .004\)).

Depression and Anxiety Symptoms in Parents of VPT vs FT Infants

Compared with parents of FT infants, parents of VPT infants had higher rates of depression shortly after birth (mothers: 6% vs 40%; odds ratio [OR] = 9.9; 95% CI, 4.3 to 23.3; \(P < .001\); fathers: 5% vs 36%; OR = 11.0; 95% CI, 4.1 to 29.6; \(P < .001\)) and at 6 months (mothers: 5% vs 14%; OR = 2.9; 95% CI, 1.0 to 8.2; \(P = .04\); fathers: 6% vs 19%; OR = 3.4; 95% CI, 1.3 to 9.0; \(P = .01\)) as well as anxiety shortly after birth (mothers: 13% vs 48%; OR = 6.5; 95% CI, 3.3 to 12.6; \(P < .001\); fathers: 10% vs 47%; OR = 7.8; 95% CI, 3.7 to 16.8; \(P < .001\)) and at 6 months (mothers: 14% vs 25%; OR = 2.1; 95% CI, 1.0 to 4.3; \(P = .05\); fathers: 10% vs 20%; OR = 2.3; 95% CI, 1.0 to 5.3; \(P = .05\)) (Table 2). When social risk and siblings were accounted for, group differences diminished, with the exception of depression in fathers.

Discussion

In our study, both mothers and fathers of VPT infants experienced elevated levels of depression and anxiety symptoms shortly after birth and their symptom levels were higher than in parents of FT infants, consistent with prior research.1,2,3 Rates of clinically significant depression and anxiety were initially high (40%-51%) in parents of VPT infants, and although rates declined during the first 12 weeks, they never dropped below 20% and always remained higher than expectations based on local general population norms (eg, for depression, 16% of women postnatally,23 and 5% and 3% in a 12-month period for all women and men, respectively).2,4 Six months after birth, mothers and fathers of VPT infants were still at higher risk for depression and anxiety than parents of FT infants, although this relationship diminished after adjustment for social and family factors.

There are several important and novel findings from our study. The first is that symptoms of depression and anxiety decreased during the newborn period for both mothers and fathers of VPT infants. Previous longitudinal studies in this population, which have focused on mothers and the postdischarge period, generally reported sustained symptoms of depression in mothers of VPT infants.3 Two studies report-
a decline used both hospitalization and postdischarge time points. Most perinatal and social characteristics had minimal effect on the relationships between time and depression or anxiety, although our study was not sufficiently powered to detect such moderating effects, another important contribution to the literature that may help to explain the mixed findings on predictors of distress in previous studies. In the general population, obstetric and perinatal complications are associated with parental depressive symptoms even after controlling for sociodemographic variables and preexisting psychopathology. Our finding that parental distress improved over time for parents of infants regardless of duration of ventilation (considered a proxy for illness severity) may be reflective of this cohort of exclusively VPT infants having an inherently high level of risk that minimized the effect of individual medical complications on parental mental health over time. There was little evidence for differences in anxiety or depression around the time of and after discharge or transfer with the exception of slightly lower anxiety in mothers, which partially accounted for the decreasing trajectory of maternal anxiety. Although anec-

![Table 2](image-url)
Evolution of Depression and Anxiety in Parents of Very Preterm Infants

Our study is the first, to our knowledge, to conduct a detailed examination of changes in distress over time in parents of VPT infants at frequent intervals during the newborn period. This is a sensitive time during which interventions may be effective. Other strengths include the cohort of parents exclusively of VPT infants and the thorough investigation of mental health in fathers. Limitations include the use of validated screening rather than diagnostic tools to measure symptoms of depression and anxiety. However, this reduced the burden for parents given the multiple assessments and provided information on symptom severity, which is important given that even subclinical symptoms of depression and anxiety are often distressing enough to warrant intervention. The high level of support services available at the hospital may have contributed to the improvement in symptoms over time, and indeed this was evident for fathers in our results. Our protocol of following up with parents who reported clinically significant symptoms may also have had an impact.

Conclusions

It is important that fathers not be overlooked after birth of VPT infants. Fathers showed high rates of depression and anxiety, comparable with those experienced by mothers. There is less awareness of the challenges faced by fathers and consequently often limited support provided to them. Although beyond the scope of this article, future research should examine how mental health in one parent influences the well-being of his or her partner. This study also identified critical times for assessment and potential intervention for parents. For example, it is clear that many mothers and fathers need support shortly after the birth of their VPT infant. While an important message for parents is that distress does improve over time, it is also noteworthy that symptoms of depression and anxiety remain elevated beyond the very early weeks after birth of VPT infants, and parents should continue to be monitored.


