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Adverse obstetric and neonatal outcomes in women with severe mental illness: To what extent can they be prevented?

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ABSTRACT

Background: Women with schizophrenia and bipolar disorder are at a higher risk of obstetric and neonatal complications. The aim of this study was to better understand the factors that may influence these adverse outcomes.
Method: We examined obstetric and neonatal outcomes of pregnant women with schizophrenia and bipolar disorder and factors possibly influencing these outcomes. A retrospective review of the medical history of 112 women with a DSM-IV diagnosis of schizophrenia or bipolar disorder was undertaken. Data for controls were extracted from the hospital's electronic birth record data.
Results: Women with schizophrenia and bipolar disorder presented later for their first antenatal visit and had higher rates of smoking and illicit drug use than the control group. They also had higher rates of pre-eclampsia and gestational diabetes. Their infants were less likely to have Apgar scores 8–10 at both 1 and 5 minutes and were more likely to be admitted to special care/neonatal intensive care nursery than the infants of controls. The rate of pre-term birth was significantly increased in the women with schizophrenia and bipolar disorder. Pre-term birth and admission to special care/neonatal intensive care were predicted by smoking and illicit drug use.
Conclusion: These data point to potentially modifiable factors as significant contributors to the high rate of adverse obstetric and neonatal outcomes in women with mental illness. Comprehensive management of women with mental illness prior to, during pregnancy and in the postnatal period may have long-term benefits for their offspring.

1. Introduction

Pregnancy and birth complications may result in a range of injuries extending from fetal and neonatal death to developmental compromise including later emotional, cognitive and behavioral problems in the child (Verdoux and Bourgeois, 1993; Schetter and Tanner, 2012; Unterscheider et al., 2014). Data linkage studies have shown that women with schizophrenia (Bennedsen et al., 2001; Nilsson et al., 2002; Jablensky et al., 2005) and bipolar disorder are at increased risk of a range of obstetric and neonatal complications (MacCabe et al., 2007; Lee and Lin, 2010; Bodén et al., 2012). Women with schizophrenia have an increased risk of pre-term birth, low birth weight and small for gestational age babies (Bennedsen et al., 2001; Nilsson et al., 2002; Jablensky et al., 2005), greater risk of placental abruption (Jablensky et al., 2005) and of infants with cardiovascular congenital abnormalities (Jablensky et al., 2005), stillbirth and infant death (Nilsson et al., 2002). Women with schizophrenia have also been shown to be at greater risk of interventions such as cesarean section, vaginal assisted delivery, and pharmacological stimulation of labor (Bennedsen et al., 2001). Women with bipolar disorder have an increased risk of preterm birth (MacCabe et al., 2007; Lee and Lin, 2010) and small or growth retarded babies (MacCabe et al., 2007; Lee and Lin, 2010; Bodén et al., 2012) as well as increased risk of placenta previa and antepartum hemorrhage (Jablensky et al., 2005). Studies have also shown that pregnancy outcomes are worse for women with schizophrenia than those with bipolar disorder (Verdoux and Bourgeois, 1993; Jablensky et al., 2005).

The cause(s) of these complications and the potential to prevent them is unclear. Possible causative factors include an abnormality in

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fetal development due to a genetic predisposition, the effects of maternal mental illness and stress, co-morbid problems such as socio-demographic disadvantage, poor nutrition and associated lifestyle factors, poor attendance at antenatal care, or the effects of prescribed drugs (Sacker et al., 1996; Jablensky et al., 2005; McColl et al., 2013). It is likely that multiple factors influence risk and mediate poor outcomes. Data sets vary in the range and detail of information available to explore causal hypotheses and the effects of potential confounding factors. In particular, information about the quality and quantity of both obstetric and mental health care provided to women during their pregnancy is usually scant.

Recently, Nguyen et al. (2012) compared obstetric and neonatal outcomes of a sample of women with severe mental illness (SMI) with general population data. Consistent with previous studies, women with SMI had a lower rate of spontaneous vaginal delivery and a higher rate overall of complications of pregnancy. In contrast with some earlier studies, women with SMI had a greater risk of gestational diabetes mellitus and pre-eclampsia. In addition, the birth weights of infants of women with SMI were similar to those in the control group, and risk of preterm birth was not significantly greater compared with controls.

A changed profile of obstetric and neonatal outcomes suggests that factors other than or in addition to genetic predisposition, may account for the higher rates of complications seen in women with SMI. If this is so, these complications may be preventable, with the potential to reduce later emotional, cognitive and behavioral problems in the children of women with SMI.

The current study was undertaken to further explore the nature of obstetric and neonatal outcomes of pregnant women with schizophrenia and bipolar disorder, as well as determine factors possibly influencing these outcomes.

2. Methods

2.1. Setting

The Royal Women's Hospital (RWH) in Melbourne, is Australia's largest specialist women's hospital, providing care to women with 'high risk' pregnancies as well as to all women living in a local catchment area. Care is delivered by four multidisciplinary teams (*Teamcare*) comprising midwives, obstetricians, a social worker, dietician, physiotherapist, physician and psychiatrist. The hospital has a multidisciplinary consultation-liaison mental health team. Women with mental health problems are seen in *Teamcare* rather than in a stand-alone or specialist clinic. All women identified in the antenatal period as having a mental health problem by maternity staff are referred to the team psychiatrist who then provides direct care to the woman and/or is involved in ongoing liaison with the woman's usual mental health care provider. The study received ethical approval by the institutional review board.

2.2. Subjects

Women who delivered a baby at the hospital were included in the study if a diagnosis of schizophrenia or bipolar disorder was made following clinical interview with the maternity team psychiatrist between August 2008 and September 2012. Diagnoses were made using DSM-IV criteria. Data were collected by retrospective file audit. A comparison sample was obtained from the hospital's electronic birth record data for the period 2009–2012. The Centricity Perinatal data recording system (GE) was first introduced at RWH in October 2009 and contains information regarding antenatal course as well as labor and delivery. Our control sample comprised all women seen for antenatal care who delivered at the hospital from 2009 to September 2012, but excluding those with schizophrenia or bipolar disorder. Hereafter, the women with schizophrenia and bipolar disorder and the comparison sample will be referred to as the study group and control group, respectively.

2.3. Data analysis

Prior to analysis, the data were examined for the assumptions of normality required for parametric tests. No violations of assumptions were found. Independent sample *t*-tests were used to compare groups on continuous measures and Pearson chi-square tests were employed for categorical data. Two separate logistic regression analyses were conducted. The first was to test predictors of the antenatal complication of pre-eclampsia and the second to test for predictors of the neonatal complication of pre-term birth. Four predictors (smoking, alcohol use, illicit drug use and having a diagnosis of either schizophrenia or bipolar disorder) were used for both logistic regression analyses. Direct logistic regression method was used whereby all four predictors were entered simultaneously into each equation. Significant predictors were identified by examining the resultant Wald test statistics, odds ratios (OR) and 95% confidence intervals (CI). A multiple regression analysis was then performed to identify whether the same set of predictors used in the logistic regression, predicted birth weight in the combined study and control group. Differences for all analyses were considered statistically significant at $p < .05$. For the chi-square tests, Fisher's exact test was reported when cell numbers were less than expected. All statistical analyses were performed using the statistical software package IBM SPSS for Windows release 21.0.

3. Results

3.1. Antenatal care

Sixty-three women with schizophrenia and 49 women with bipolar disorder were seen during the period of interest. The pregnancies resulted in 110 singleton births and two twin births. One twin in one of the sets was stillborn. The control sample identified comprised 19,755 women. As can be seen in Table 1, the women in the study group were, on average, older and presented for their first antenatal visit significantly later in their gestation (18.8 weeks) compared to the control group (15.1 weeks). Women in the study group attended a mean of 8.8 ($\pm$3.6) antenatal visits. This same information regarding the control population was unavailable for comparison. Smoking, alcohol use and illicit drug use were all significantly higher among the study group compared to the controls.

The same comparison was then undertaken between the women with schizophrenia and bipolar disorder. There were few differences between the two groups except that antenatal therapeutic drug exposure was significantly different between the two disorders. Although antipsychotic medications were the most commonly prescribed drug for both groups, the women with schizophrenia were significantly more likely to take these medications than the bipolar group (65% vs. 43%, $p = .02$). Women with schizophrenia attended their first antenatal visit a little later than did those with bipolar disorder (19.7 $\pm$ 8.4 weeks vs. 17.6 $\pm$ 7.0) and alcohol use, smoking and illicit drug use in pregnancy was higher in the group with schizophrenia than those with bipolar disorder, but these differences did not reach statistical significance.

Just under 10% of women with schizophrenia or bipolar disorder, were admitted to an acute psychiatric unit during their pregnancy (12.7% with schizophrenia and 6.1% with bipolar disorder). Following the birth of their baby, 20.6% of women with schizophrenia and 10.2% with bipolar disorder were admitted with their infant to a mother baby psychiatric unit. Statutory child welfare services were significantly ($p < .001$) more likely to be involved with women with schizophrenia (34.9%) than those with bipolar disorder (8.2%).

3.2. Obstetric outcomes

The study group had significantly more obstetric complications than controls. Women with schizophrenia and bipolar disorder had