Obstetric and neonatal outcomes of pregnant women with severe mental illness at a specialist antenatal clinic

Thinh N Nguyen
MB BS, FRANZCP,
CertChildAdolPsych,
Consultant Psychiatrist,
and Clinical Senior
Lecturer[1,4]

Deb Faulkner
MPsych, PhD,
Project Officer[2]

Jacqueline S Frayne
MB BS, DRANZCOG,
FRACGP,
Obstetrics Medical
Officer[1]

Suzanna Allen
RN, RM, BScN,
Clinical Midwife[1]

Yvonne L Hauck
BScN, MSc, PhD,
Professor of Midwifery
(Joint Appointment),[1,3]
and Research
Consultant[2]

Daniel Rock
PhD, FRSPH,
Director,[2] and
Clinical Professor[4]

Jonathan Rampono
MB BS, FRANZCP,
Consultant Psychiatrist,[1]
and Head of Department
of Psychological
Medicine[4]

1 King Edward Memorial
Hospital, Perth, WA.

2 Clinical Applications
Unit, Centre for Clinical
Research in
Neuropsychiatry,
Graylands Hospital,
Perth, WA.

3 Curtin University,
Perth, WA.

4 University of Western
Australia, Perth, WA.

nguyent@
meddent.uwa.edu.au

Increased morbidity and mortality trends in patients with severe mental illness (SMI), coupled with suboptimal access to health provision,[1] highlights the need for comprehensive yet individualised care. Pregnant women with SMI and their babies appear to be a particularly vulnerable group, due to increased risks for obstetric and neonatal complications.[2-4] In a Western Australian population study,[3] women with schizophrenia and major affective disorders were more likely to experience placental abnormalities and fetal distress. Women with schizophrenia were also more likely to have newborns in the lowest weight/growth decile and have a neonatal narcotic antagonist administered.

Pregnant women with bipolar disorder have been found to be at increased risk of preterm and low-birthweight infants.[5,6] Mothers with SMI present with poor maternal condition,[7] which is reflected by late presentation to obstetric services and fewer appointments,[8,9] poor nutrition, more likelihood of smoking, illicit substance use, and less support.[10,11] Additional concerns include antipsychotic exposure during pregnancy, which has been associated with fetal malformation;[12] infant growth disruption; increased or decreased birthweight;[12,13] and neonatal adjustment difficulties.[14]

Pregnant women with SMI should be designated as a health disparity population,[15] and every effort should be made to improve their access to obstetric care. Within this context, the Childbirth and Mental Illness Antenatal Clinic (CAMI clinic) at King Edward Memorial Hospital (KEMH) was established in 2007. The weekly antenatal clinic comprises a multidisciplinary team of designated obstetrics, midwifery, psychiatry, mental health nursing and social work staff who provide care for pregnant women, in liaison with their treating psychiatrists. This approach has the potential to increase attendance at antenatal care for pregnant women with SMI.[16]

We report on the obstetric and neonatal outcomes of pregnant women with SMI who attended the CAMI clinic between 2007 and 2011.

Method

A retrospective file audit was made of all pregnant women with SMI who attended the CAMI clinic and gave birth between December 2007 and April 2011. Psychiatric diagnoses were grouped into schizophrenia and related disorders, bipolar disorders, and non-psychotic disorders with significant functional impairment. Diagnoses were made by community mental health services, private psychiatrists or a consultant psychiatrist at KEMH using ICD-10 criteria.[17]

Abstract

Objective: To evaluate the obstetric and neonatal outcomes of pregnant women with severe mental illness (SMI) who attended a specialist multidisciplinary antenatal clinic in Perth, Western Australia.

Design, setting and participants: A retrospective case-note audit of outcomes from the Childbirth and Mental Illness Antenatal Clinic (CAMI clinic) at King Edward Memorial Hospital for pregnant women with severe mental illness (SMI), aged 18–41 years, who gave birth between December 2007 and April 2011, and their babies.

Main outcome measures: Obstetric and neonatal outcomes for 138 women and newborns from singleton live births. Data were compared between three diagnostic groups (schizophrenia, bipolar and non-psychotic SMI), and with WA obstetric and perinatal statistics for 2008.

Results: 44 women with schizophrenia, 56 with bipolar disorder and 38 with non-psychotic SMI attended antenatal care for an average of 7.7 (SD, 3.3) visits. The proportion of women who smoked tobacco was significantly higher than that in the WA antenatal population (46% v 15%; $P < 0.0001$). Alcohol use, illicit substance use and psychotropic medication exposure during pregnancy were high. The women were at increased risk of developing gestational diabetes mellitus (15% v 4%; $P < 0.0001$) and pre-eclampsia (9% v 3%; $P < 0.0001$), and birth complications were more common. Babies born to CAMI clinic women were less likely to have Apgar scores $\geqslant 8$ at 1 minute and 5 minutes. Pregnant women with schizophrenia had more psychiatric relapses during pregnancy, and had more statutory child welfare involvement. Gestational age at birth and infant birth weights were similar for the pregnant women with SMI and the WA population in 2008.

Conclusions: Women attending our specialist clinic had increased rates of obstetric and neonatal complications compared with the general population, and were exposed to a cluster of risk factors. We report encouraging trends in antenatal attendance, gestational age at birth, and birth weights. Managing pregnant women with SMI will require a comprehensive approach aimed at early detection of obstetric complications and psychosocial difficulties, as well as neonatal monitoring. Optimising prepregnancy maternal health and welfare may also be of benefit.

Data audited from case notes were based on the Western Australian Midwives' Notification System. The purpose-designed database also included psychiatric diagnoses, detailed demographic information, attendance at the CAMI clinic (including the number of antenatal appointments), psychotropic medication use, and psychosocial outcomes, including psychiatric admissions and statutory welfare agency involvement. The KEMH Ethics Committee approved the study.

Statistical analysis

CAMI clinic data (summary data from all women combined) were compared with obstetric and perinatal

1 Obstetric complications among women attending the Childbirth and Mental Illness Antenatal Clinic (CAMI clinic) and in the Western Australian population, 2008

	Schizophrenia (n = 44)	Bipolar disorder (n = 56)	Non-psychotic SMI* (n = 38)	P	CAMI clinic (n = 138)	WA (n = 29 805)	P
Complications of pregnancy							
Threatened preterm labour	4 (9.1%)	4 (7.1%)	1 (2.6%)	0.483	9 (6.5%)	747 (2.5%)	0.006
Pre-eclampsia	3 (6.8%)	6 (10.7%)	3 (7.9%)	0.773	12 (8.7%)	792 (2.7%)	< 0.0001
Antepartum haemorrhage	4 (9.1%)	2 (3.6%)	2 (5.3%)	0.496	8 (5.8%)	1056 (3.5%)	0.232
Gestational diabetes	9 (20.5%)	7 (12.5%)	5 (13.2%)	0.501	21 (15.2%)	1322 (4.4%)	< 0.0001
No complications	16 (36.4%)	19 (33.9%)	14 (36.8%)	0.949	49 (35.5%)	20 450 (68.6%)	< 0.0001
Type of birth							
Spontaneous vaginal delivery	14 (31.8%)	26 (46.4%)	18 (47.4%)	0.250	58 (42.0%)	15 781 (52.9%)	0.013
Instrumental	7 (15.9%)	16 (28.6%)	6 (15.8%)	0.198	29 (21.0%)	4098 (13.7%)	0.019
Elective caesarean	5 (11.4%)	7 (12.5%)	13 (34.2%)	0.010	25 (18.1%)	5347 (17.9%)	0.954
Emergency caesarean	18 (40.9%)	7 (12.5%)	1 (2.6%)	< 0.0001	26 (18.8%)	4453 (14.9%)	0.245
Complications of labour and delivery							
Suspected fetal distress	18 (40.9%)	12 (21.4%)	9 (23.7%)	0.076	39 (28.3%)	3768 (12.6%)	< 0.0001
Postpartum haemorrhage	5 (11.4%)	10 (17.9%)	4 (10.5%)	0.512	19 (13.8%)	3500 (11.7%)	0.546
Shoulder dystocia	2 (4.5%)	3 (5.4%)	1 (2.6%)	0.814	6 (4.3%)	482 (1.6%)	0.028
Delay to progress < 3 cm	5 (11.4%)	1 (1.8%)	1 (2.6%)	0.069	7 (5.1%)	1206 (4.0%)	0.694
Delay to progress > 3 cm	14 (31.8%)	11 (19.6%)	5 (13.2%)	0.110	30 (21.7%)	1701 (5.7%)	< 0.0001
No complications	10 (22.7%)	27 (48.2%)	10 (26.3%)	0.014	47 (34.1%)	11 675 (39.2%)	0.254

SMI = severe mental illness. * Diagnoses: recurrent major depressive disorder (15); emotionally unstable personality disorder (12); generalised anxiety disorder (4); post-traumatic stress disorder (3); severe adjustment disorder (2); anorexia nervosa (1); panic disorder (1). ◆

data from the Midwives' Notification System in 2008[18] using t tests for normally distributed, continuous variables, and the χ^2 test for categorical data. Comparisons between CAMI clinic women and the WA population were made using WA singleton pregnancies where data were available (n = 29 805). Our sample size provided 80% power to detect a 3% overall difference in proportions comparing against the WA population. Where WA singleton data were not separately reported, we compared our sample with data for 30 234 pregnancies across the state. Different diagnostic groups within the CAMI clinic data were compared using one-way analysis of variance for normally distributed, continuous variables, the Kruskal–Wallis test for non-normally distributed continuous variables, and the χ^2 test for categorical data. Normality was determined using a Kolmogorov–Smirnov test with $P < 0.05$ considered significant. Proportion of optimal birthweight (POBW) was calculated using the formula in Blair and colleagues.[19]

Results

One hundred and forty-two CAMI clinic women gave birth between December 2007 and April 2011. Four women had two consecutive pregnancies during this period, two had twin pregnancies, one fetal death occurred, and one pregnancy was terminated due to fetal chromosomal abnormalities. Data presented are the outcomes for 138 women and newborns from first presentation to the clinic to a live singleton birth. Of these, 44 women were diagnosed with schizophrenia, 56 with bipolar disorder and 38 with non-psychotic SMI.

The mean age of the women attending the clinic was 28.9 years (SD, 5.5), which was similar to that of women in the WA population (29.5 years; SD, 5.8). A greater proportion of women was nulliparous (52% v 41%, respectively; $P = 0.012$), and presented with higher smoking rates (46% v 15.4%, respectively; $P < 0.0001$). Women with schizophrenia were less likely to have a regular general practitioner recorded, compared with the other diagnostic groups ($P = 0.013$).

Antenatal care

Among three diagnostic categories of women attending the clinic, maternal age, gestation at first appointment, gravidity, and parity were similar. For all groups, the mean body mass index (BMI) at first antenatal appointment was in the overweight to obese range (mean [SD], 29.1 [6.8]). Among the study women, there was a high rate of alcohol use (19.6%), as well as illicit substance use (25.4%), during pregnancy. Illicit substance use was more prevalent for women with schizophrenia (40.9%) compared with the other two groups ($P = 0.006$). The women attending our clinic also had high rates of exposure to antipsychotics (mostly atypical) at any time during pregnancy (93.2%, 76.8% and 42.1% for schizophrenia, bipolar and non-psychotic SMI, respectively; $P < 0.0001$).

In our study, women with a diagnosis of schizophrenia had greater non-attendance to antenatal care than women with bipolar disorder and non-psychotic SMI (mean proportion of appointments attended: 84%, 95%, 92%, respectively; $P = 0.02$). However, the actual mean numbers of appointments attended were similar across

2 Neonatal outcomes for babies of women attending the Childbirth and Mental Illness Antenatal Clinic (CAMI clinic), compared with the Western Australian population, 2008

	Schizophrenia (n = 44)	Bipolar disorder (n = 56)	Non-psychotic SMI* (n = 38)	P	CAMI clinic (n = 138)	WA (n = 30 234)†	P
Apgar score							
8–10 at 1 min	28 (63.6%)	36 (64.3%)	28 (73.7%)	0.558	92 (66.7%)	25 822 (84.9%)	< 0.0001
< 4 at 1 min	2 (4.5%)	2 (3.6%)	1 (2.6%)	0.898	5 (3.6%)	514 (1.7%)	0.154
8–10 at 5 min	40 (90.9%)	50 (89.3%)	35 (92.1%)	0.896	125 (90.6%)	29 683 (97.5%)	< 0.0001
Mean baby weight, grams (SD)	3356 (809)	3342 (639)	3415 (507)	0.865	3366 (663)	3341 (607)	0.629
Excluding smokers‡	3590 (484)	3539 (693)	3370 (478)	0.429	3506 (579)		
Mean POBW (SD)	0.989 (0.169)	0.978 (0.123)	0.995 (0.131)	0.832	0.986 (0.140)		
Mean gestation at birth, weeks (SD)	38.69 (2.78)	38.85 (2.48)	38.80 (1.53)	0.947	38.79 (2.35)		
Preterm births (< 37 weeks)	5 (11.4%)	5 (8.9%)	2 (5.3%)	0.618	12 (8.7%)	2093 (7.0%)	0.548
Special Care Nursery admission	19 (43.2%)	14 (25.0%)	11 (28.9%)	0.138	44 (31.9%)		
Department for Child Protection involvement	22 (50%)	8 (14.3%)	9 (23.7%)	0.0003	39 (28.3%)		

POBW = proportion of optimal birth weight. SMI = severe mental illness. * Diagnoses: recurrent major depressive disorder (15); emotionally unstable personality disorder (12); generalised anxiety disorder (4); post-traumatic stress disorder (3); severe adjustment disorder (2); anorexia nervosa (1); panic disorder (1). † Singleton data not separately reported. Total recorded Apgar scores in WA population at 1 min (n = 30 427); total recorded Apgar scores at 5 min (n = 30 431). ‡ Non-smokers: schizophrenia (n = 22); bipolar disorder (n = 31); non-psychotic SMI (n = 21). ◆

all diagnostic groups (mean appointments attended [SD], 7.7 [3.3]).

Obstetric outcomes

Women attending the CAMI clinic were at increased risk of developing gestational diabetes mellitus (GDM) (15.2% v 4.4%: $P < 0.0001$), pre-eclampsia (8.7% v 2.7%; $P < 0.0001$), and threatened preterm labour (6.5% v 2.5%; $P = 0.006$) compared with women from the general WA obstetric population. Our sample was also less likely to be free of complications of pregnancy (Box 1).

Complications of labour and delivery were more common for women attending the CAMI clinic compared with the 2008 WA population data. In particular, suspected fetal distress was significantly more common (28.3% v 12.6%; $P < 0.0001$), as was delay to progress (> 3 cm) (21.7% v 5.7%; $P < 0.0001$). High rates of suspected fetal distress were reflected in the high rates of non-elective (emergency) caesarean births, particularly in the women with schizophrenia (40.9%); however, the overall rate of emergency caesarean was not significantly different (18.8% v 14.9%).

Neonatal outcomes

Neonatal outcomes are shown in Box 2. One baby born to a mother with schizophrenia had a patent ductus arteriosus, which was treated conservatively. Babies born to women attending the CAMI clinic were less likely to have an Apgar score $\geqslant 8$ at 1 minute (67% v 85%; $P < 0.0001$), and were also less likely to have an Apgar score $\geqslant 8$ at 5 minutes (91% v 98%; $P < 0.0001$). Furthermore, special care nursery admissions were high (31.9%). Birthweights were about equivalent for the study infants and the general population (3366 g and 3341 g, respectively; $P = 0.629$). The mean POBW among the babies born to women attending the CAMI clinic was 0.986 (SD, 0.140), where 1 is considered optimal. There was no significant difference in POBW between diagnostic groups.

Psychosocial outcomes

Psychiatric relapses during pregnancy were common, with 22.5% of women being admitted to a psychiatric hospital during pregnancy. Psychiatric admission rates were higher for women with schizophrenia than for women with bipolar disorder and other diagnoses (38.6%, 10.7% and 21.1%, respectively; $P = 0.004$). Women with schizophrenia also had significantly higher rate of involvement of statutory child welfare services (Department for Child Protection) than women with bipolar disorder or non-psychotic SMI (50%, 14.3% and 23.7%, respectively; $P = 0.0003$).

Discussion

Our results confirm previous large-scale data linkage studies, indicating that pregnant women with SMI, particularly women with schizophrenia, remain at risk of obstetric complications. In contrast with the study by Jablensky and colleagues,[3] conducted on the WA population between 1980 and 1992, our cohort represents a possible change in the profile of obstetric risks for pregnant women with SMI, with high mean maternal BMI at booking, increasing rates of GDM, pre-eclampsia, and neonatal adjustment difficulties within the context of relatively normal infant birthweights.

There are limited reports on associations between GDM and maternal exposure to antipsychotics during pregnancy.[12,20] The rate of GDM in women attending our clinic (15.2%) was more than three times that for WA (4.4%). Our findings also highlighted an increased risk of pre-eclampsia compared with the overall population, which is in contrast with previous studies.[2,3] These findings suggest a potential metabolic vulnerability in pregnant women with SMI, as pre-eclampsia and GDM share similar pathophysiological abnormalities and may relate to insulin resistance, a feature of metabolic syndrome, which is prevalent among patients with psychotic disorders.[1]

Increased rates of pre-eclampsia must be considered in the context of an increased proportion of nulliparity in the study sample, which increases the risk for pre-eclampsia, and the high rate of smoking, which is known to reduce it.[21] The high mean maternal BMI at booking for our diagnostic groups may have influenced obstetric outcomes, as high maternal BMI is associated with gestational diabetes, pre-eclampsia and macrosomia.[22]

The primary strength of our study was that we examined in detail pregnant women with SMI in relation to their multifactorial risk profiles. In particular, we examined additional variables such as attendance at antenatal care, which is not routinely collected or available in data-linkage studies. The main limitation was a lack of a matched control group, which limited the assessment of this specialised care compared with routine care. In addition, post-hoc analyses found a number of our null findings were insufficiently powered, which may have masked the detection of some, necessarily small, differences in specific obstetric complication rates.

Women with schizophrenia gave birth to infants with mean birthweights not significantly different from those of the other diagnostic groups, and overall, the study sample had a similar mean birthweight to that of the WA population, even when smoking was accounted for. This contrasts with a number of studies that found that babies born to mothers with schizophrenia tended to have lower mean birthweight.[2,3] A number of factors may account for these changes, including attendance to antenatal care, exposure to atypical antipsychotics, and increased maternal BMI. These factors may balance out the effects of the illness and smoking in terms of birthweight and preterm births.

In addition to an increased rate of suspected fetal distress, our findings showed that babies of women with SMI have poorer adjustment in the postpartum period, with relatively lower Apgar scores and higher rates of special care nursery admission. Compared with other findings,[3] the women in our study did not have any documented narcotic reversal usage, which could suggest an increasing awareness of neonatal adjustment difficulties and the need for observation and conservative management.

Psychiatric relapses requiring inpatient admission were reported in over a fifth of women attending our clinic, and women with schizophrenia were more vulnerable. This may not only influence obstetric complications but adds to the complexities of antenatal management, in particular the need for close liaison between psychiatric and obstetric services. Similarly, the high rate of involvement of child welfare services in women with schizophrenia is in keeping with previous findings[23] and reflects the disruptive nature of this condition on all facets of wellbeing and function. It further highlights the need for comprehensive multidisciplinary antenatal care with social work involvement and appropriate planning for the postpartum period.

1 De Hert M, Correll CU, Bobes J, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry* 2011; 10: 52-77.

2 Bennedsen BE, Mortensen PB, Olesen AV, et al. Obstetric complications in women with schizophrenia. *Schizophr Res* 2001; 47: 167-175.

3 Jablensky AV, Morgan V, Zubrick SR, et al. Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders. *Am J Psychiatry* 2005; 162: 79-91.

4 Nilsson E, Lichtenstein P, Cnattingius S, et al. Women with schizophrenia: pregnancy outcome and infant death among their offspring. *Schizophr Res* 2002; 58: 221-229.

5 MacCabe JH, Martinsson L, Lichtenstein P, et al. Adverse pregnancy outcomes in mothers with affective psychosis. *Bipolar Disord* 2007; 9: 305-309.

6 Lee HC, Lin HC. Maternal bipolar disorder increased low birthweight and preterm births: a nationwide population-based study. *J Affect Disord* 2010; 121: 100-105.

7 Abel KM, Morgan V. Mental illness, women, mothers and their children. In: Tsuang MT, Tohen M, Jones PB, editors. Textbook in psychiatric epidemiology. John Wiley & Sons; 2011: 483-507.

8 Miller LJ, Finnerty M. Sexuality, pregnancy, and childrearing among women with schizophrenia-spectrum disorders. *Psychiatr Serv* 1996; 47: 502-506.

9 Goodman SH, Emory EK. Perinatal complications in births to low socioeconomic status schizophrenic and depressed women. *J Abnorm Psychol* 1992; 101: 225-229.

10 Miller LJ. Sexuality, reproduction, and family planning in women with schizophrenia. *Schizophr Bull* 1997; 23: 623-635.

11 Abel KM, Webb RT, Salmon MP, et al. Prevalence and predictors of parenting outcomes in a cohort of mothers with schizophrenia admitted for joint mother and baby psychiatric care in England. *J Clin Psychiatry* 2005; 66: 781-789.

12 Reis M, Källén B. Maternal use of antipsychotics in early pregnancy and delivery outcome. *J Clin Psychopharmacol* 2008; 28: 279-288.

13 Newham JJ, Thomas SH, MacRitchie K, et al. Birth weight of infants after maternal exposure to typical and atypical antipsychotics: prospective comparison study. *Br J Psychiatry* 2008; 192: 333-337.

14 Newport DJ, Calamaras MR, DeVane CL, et al. Atypical antipsychotic administration during late pregnancy: placental passage and obstetrical outcomes. *Am J Psychiatry* 2007; 164: 1214-1220.

15 De Hert M, Cohen D, Bobes J, et al. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. *World Psychiatry* 2011; 10: 138-151.

16 Nguyen TN, Faulkner D, Allen S, et al. Managing pregnant women with serious mental illness: using the Edinburgh Postnatal Depression Scale as a marker of anxiety and depressive symptoms. *Aust N Z J Psychiatry* 2010; 44: 1036-1042.

17 World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders. Clinical descriptions and diagnostic guidelines. Geneva: WHO, 1992.

18 Le M, Tran BN. Perinatal Statistics in Western Australia, 2008. Twenty-sixth Annual Report of the Western Australian Midwives' Notification System. Perth: Government of Western Australia Department of Health, 2008. http://www.health.wa.gov.au/publications/subject_index/p/Perinatal_infant_maternal.cfm (accessed Feb 2012).

19 Blair EM, Liu Y, de Klerk NH, Lawrence DM. Optimal fetal growth for the Caucasian singleton and assessment of appropriateness of fetal growth: an analysis of a total population perinatal database. *BMC Pediatr* 2005; 5: 13.

20 McCauley-Elsom K, Gurvich C, Elsom SJ, Kulkarni J. Antipsychotics in pregnancy. *J Psychiatr Ment Health Nurs* 2010; 17: 97-104.

21 North RA, McCowan LM, Dekker GA, et al. Clinical risk prediction for pre-eclampsia in nulliparous women: development of model in international prospective cohort. *BMJ* 2011; 342: d1875. doi: 10.1136/bmj.d1875.

22 Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. *Obstet Gynecol* 2011; 118: 305-312.

23 Park JM, Solomon P, Mandell DS. Involvement in the child welfare system among mothers with serious mental illness. *Psychiatr Serv* 2006; 57: 493-497. ❏