ORIGINAL ARTICLE

Perinatal outcomes of women with gestational breast cancer in Australia and New Zealand: A prospective population-based study

Elizabeth Sullivan MD, FAFPHM[1] | Nadom Safi MBChB, MPH, DRMR (Rheumatology), PhD[1] | Zhuoyang Li BMed, MPH, PhD[1] | Marc Remond PhD[1] | Tina Y. T. Chen MBChB, PhD[2] | Nasrin Javid RM, MMedSc, PhD[2] | Jan E. Dickinson MD, FRANZCOG[3] | Angela Ives MSc, PhD[4] | Karin Hammarberg RN, PhD[5] | Antoinette Anazodo MBBS, MSC, PhD[6] | Frances Boyle MBBS (Hons I), FRACP, PhD[7] | Jane Fisher PhD, MAPS[5] | Lesley Halliday BSc, PhD[8] | Greg Duncombe MBBS, FRANZCOG[9] | Claire McLintock MBChB, FRACP[10] | Alex Y. Wang MPH, PhD[2] | Christobel Saunders MBBS, FRCS, FRACS[3]

[1]College of Health, Medicine and Wellbeing, University of Newcastle, Newcastle, New South Wales, Australia

[2]Faculty of Health, University of Technology Sydney, Sydney, New South Wales, Australia

[3]Faculty of Health and Medical Sciences, The University of Western Australia, Perth, Western Australia, Australia

[4]Faculty of Health and Medical Sciences, Medical School, The University of Western Australia, Perth, Western Australia, Australia

[5]School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

[6]School of Women and Children, University of New South Wales, Sydney, New South Wales, Australia

[7]Patricia Ritchie Centre for Cancer Care and Research, Mater Hospital Sydney, and University of Sydney, Sydney, New South Wales, Australia

[8]School of Public Health and Community Medicine, University of New South Wales, Sydney, New South Wales, Australia

[9]Faculty of Medicine, Centre for Clinical Research, University of Queensland, Brisbane, Queensland, Australia

[10]National Women's Health, Auckland City Hospital, Auckland, New Zealand

Correspondence
Elizabeth Sullivan, University of Newcastle, 130 University Drive, Callaghan, NSW 2308, Australia.
Email: e.sullivan@newcastle.edu.au

Abstract

Objective: To determine the epidemiology, clinical management, and outcomes of women with gestational breast cancer (GBC).

Methods: A population-based prospective cohort study was conducted in Australia and New Zealand between 2013 and 2014 using the Australasian Maternity Outcomes Surveillance System (AMOSS). Women who gave birth with a primary diagnosis of breast cancer during pregnancy were included. Data were collected on demographic and pregnancy factors, GBC diagnosis, obstetric and cancer management, and perinatal outcomes. The main outcome measures were preterm birth, maternal complications, breastfeeding, and death.

[correction added on May 13, 2022, after first online publication: CAUL funding statement was added.]

Results: Forty women with GBC (incidence 7.5/100 000 women giving birth) gave birth to 40 live-born babies. Thirty-three (82.5%) women had breast symptoms at diagnosis. Of 27 women diagnosed before 30 weeks' gestation, 85% had breast surgery and 67% had systemic therapy during pregnancy. In contrast, all 13 women diagnosed from 30 weeks had their cancer management delayed until postdelivery. There were 17 preterm deliveries; 15 were planned. Postpartum complications included the following: hemorrhage (n = 4), laparotomy (n = 1), and thrombocytopenia (n = 1). There was one late maternal death. Eighteen (45.0%) women initiated breastfeeding, including 12 of 23 women who had antenatal breast surgery. There were no perinatal deaths or congenital malformations, but 42.5% of babies were preterm, and 32.5% were admitted for higher-level neonatal care.

Conclusions: Gestational breast cancer diagnosed before 30 weeks' gestation was associated with surgical and systemic cancer care during pregnancy and planned preterm birth. In contrast, cancer treatment was deferred to postdelivery for women diagnosed from 30 weeks, reflecting the complexity of managing expectant mothers with GBC in multidisciplinary care settings.

KEYWORDS

breast cancer, breast surgery, breastfeeding, pregnancy, preterm, systemic therapy

1 | INTRODUCTION

Although the diagnosis of cancer in pregnant women is rare, it presents cross-disciplinary challenges in providing comprehensive care for the health and well-being of women and their babies.[1–4]

Breast cancer is one of the most commonly diagnosed cancers in pregnancy.[1,5,6] In European studies, estimates of incidence range from 17.5 to 37.4 per 100 000 pregnancies.[5,7] In Australia, the incidence of pregnancy-associated breast cancer, comprising breast cancer diagnosed during pregnancy or in the first year postpartum, has been estimated at 23.6 to 28.8 cases per 100 000 pregnancies. Up to one-third of these cases are diagnosed during pregnancy (gestational breast cancer [GBC]).[2,8] We previously analyzed population health data from New South Wales, Australia, and estimated GBC incidence as 6.8 per 100 000 women giving birth.[9]

Little data are available on pregnancy and maternal morbidity and mortality associated with GBC. In Australia and New Zealand, there have been no prospective, national, population-based observational studies examining the impact of GBC management on pregnancy outcomes.

This study aimed to determine the incidence, timing of diagnosis, obstetric and cancer management, and perinatal outcomes of women with GBC in Australia and New Zealand.

2 | METHODS

A binational, population-based prospective cohort study was conducted in Australia and New Zealand using the Australasian Maternity Outcomes Surveillance System (AMOSS).[10,11]

2.1 | Case definition

A case of GBC was defined as a woman giving birth with pathology-confirmed primary breast cancer that was diagnosed during pregnancy. Birth was defined as the birth of one or more live or stillborn infants weighing ≥400 g or born at ≥20 weeks' gestation. As we aimed to investigate the impact of first-time diagnosed GBC on pregnancy care and birth outcomes, women with a recurrent diagnosis of breast cancer, or those diagnosed postpartum, were excluded as were women who had a miscarriage or termination of pregnancy.

2.2 | Case identification

The AMOSS data collection methods have been described previously.[11] Women with GBC were identified by AMOSS data collectors using multiple sources including review of

routinely collected hospital data, audit committees, clinician notification, and requests to clinicians potentially caring for patients with GBC (Figure S1). Case identification and data collection were undertaken at participating AMOSS sites between January 1, 2013, and June 30, 2014.

2.3 | Data collection

A study-specific case report form (CRF) was developed, reviewed, and piloted with two breast cancer nurse consultants. Data items collected included the following: demographic and pregnancy characteristics, breast cancer diagnosis, obstetric and oncological management, and maternal and neonatal outcomes. AMOSS data collectors completed CRFs with follow-up and data quality assurance being performed by the research team.

2.4 | Outcome measures

The main outcome measures were preterm birth, maternal complications, breastfeeding, death, and model of care. A therapeutic preterm birth was defined as giving birth by labor induction or no-labor CS before 37 weeks' gestation. The details of maternal models of care in Australia are provided in Table S1.[12]

2.5 | Statistical analysis

Descriptive statistics for nominal data are presented as counts and percentages, whereas continuous measures are presented as mean and standard deviation for normal data and median, range, and interquartile range for non-normal data. The estimated GBC incidence was calculated with 95% confidence interval (CI). Denominators used for these calculations were based on pro-rata 2013-2014 birth data from Australia and New Zealand.[13–16] The chi-squared and the Fisher exact tests were used to compare outcomes between women having a preterm (<37 weeks' gestation) or term birth. A *P*-value <.05 was used to infer statistical significance. Data were analyzed using SPSS, version 24.0 (IBM Corporation).

3 | RESULTS

3.1 | Incidence

A total of 40 women with a primary diagnosis of GBC met inclusion criteria. The estimated overall incidence of GBC was 7.5 (95% CI 5.5-10.3) per 100 000 women giving birth

TABLE 1 Demographic characteristics of 40 women with gestational breast cancer, Australia and New Zealand, 2013-2014

Demographic characteristics	No. (%)
Country	
Australia	32 (80.0%)
New Zealand	8 (20.0%)
Age, years	
<30	4 (10.0%)
30-34	13 (32.5%)
35-39	19 (47.5%)
≥40	4 (10.0%)
Body mass index[a]	
<25	25 (62.5%)
25-29	7 (17.5%)
≥30	6 (15.0%)
Not known	2 (5.0%)
Type of hospital	
Public	27 (67.5%)
Private	13 (32.5%)
Parity	
0	17 (42.5%)
1	9 (22.5%)
≥2	14 (35.0%)
Smoking status	
Never smoked	23 (57.5%)
Quit smoking before becoming pregnant	7 (17.5%)
Smoking during pregnancy	3 (7.5%)
Not known	7 (17.5%)

[a] Measured at the first antenatal visit.

(7.2 (95% CI 5.1-10.2) per 100 000 in Australia and 9.0 (95% CI 4.6-17.8) per 100 000 in New Zealand). The age-specific incidence was 1.7/100 000 women aged <30 years giving birth, increasing to 20.3/100 000 for women aged 35 to 39 years.

3.2 | Demographics and diagnosis of GBC

Table 1 presents the demographic characteristics of the 40 women included in the study. The median age was 35 years (range 23-42, IQR 33-37), and 42.5% were nulliparous. The median gestational age at diagnosis was 20 weeks (range 4-40, IQR 35.25-38.75). Seven (17.5%) women were diagnosed in the first trimester (<14 weeks), 18 (45.0%) in the second trimester (14-27 weeks), and 15 (37.5%) in the third trimester (≥28 weeks) (Figure 1).

Thirty-three women (82.5%) experienced breast symptoms before confirmed diagnosis (Table 2), with a median
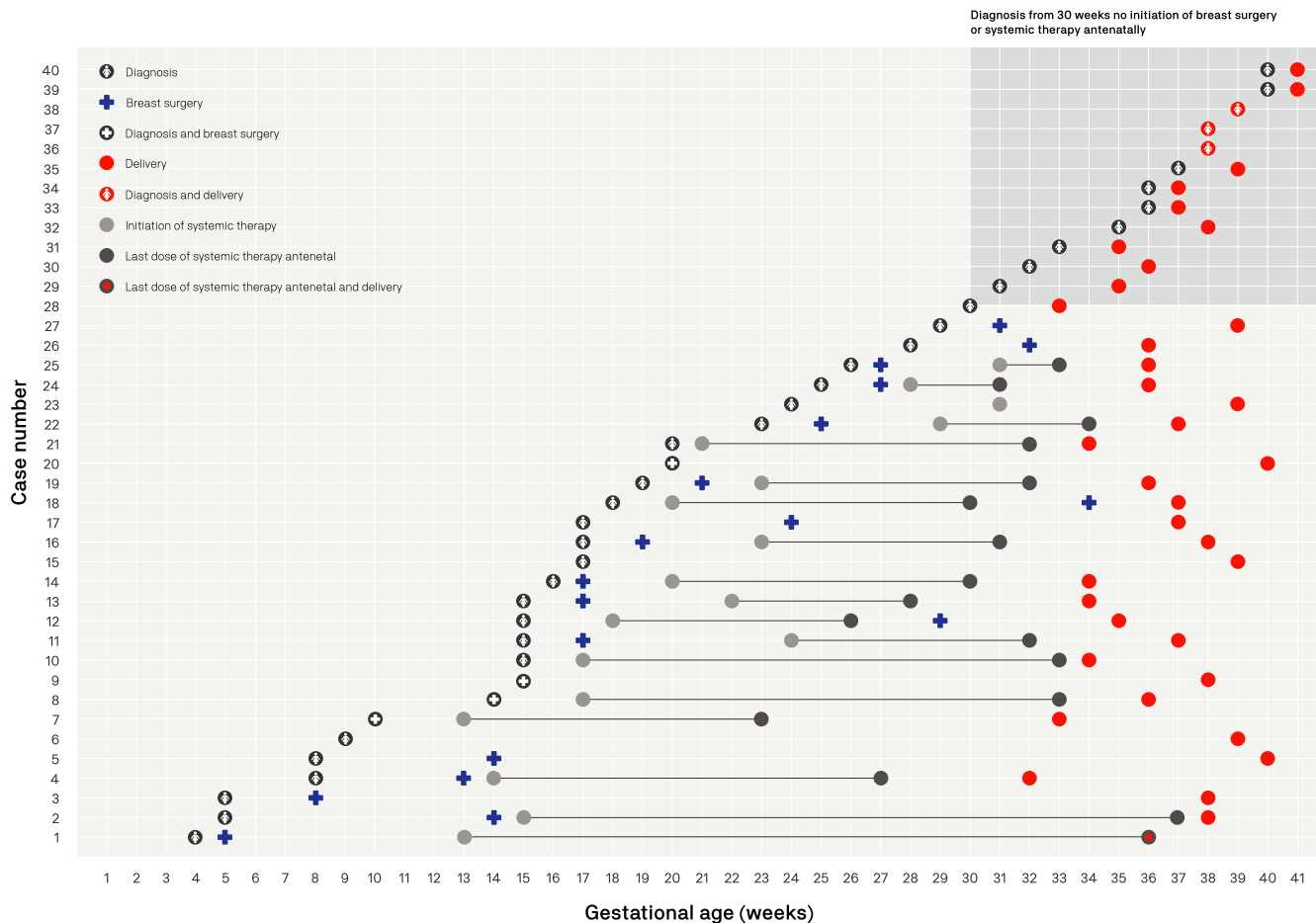
FIGURE 1 Summary of cancer management of the women with GBC. GBC, gestational breast cancer [Color figure can be viewed at wileyonlinelibrary.com]

duration of symptoms prediagnosis being 2 weeks (range 1-12, IQR 2-8). Of these women, 22 (66.7%) had a painless lump with no other symptoms, whereas 11 (33.3%) had a breast lump accompanied by symptoms including swelling, pain, breast tenderness, breast erythema, nipple discharge, nipple retraction, and peau d'orange.

3.3 | Model of care

The most frequent initial models of maternity care provided to included women were as follows: private obstetrician (specialist) care for 10 (25%) women, public hospital maternity care for 8 (20.0%), high-risk public hospital maternity care for 4 (10.0%), and shared care for 4 (10%). In addition, general practitioner obstetrician care was provided for 2 (5.0%) women, midwifery group practice caseload care for 2 (5.0%) women, and team midwifery care and combined care for 2 (5.0%) women. The model of care was not reported for 8 (20.0%) women. During pregnancy, the model of care provided was changed for seven women: Four changed to high-risk public hospital maternity care,

two to public hospital maternity care, and one to private obstetrician (specialist) care. The two women who initially selected general practitioner obstetrician care opted for high-risk public hospital maternity care later in their pregnancies. The most common models of care provided at the time of birth were graduated multidisciplinary public hospital care models for 17 (42.5%) women (comprising routine public hospital maternity care for 9 (22.5%) and high-risk public hospital maternity care for 8 (20.0%)) and private obstetrician (specialist) care for 11 (27.5%) women.

3.4 | Management of GBC

Twenty-three (57.5%) women underwent surgery during pregnancy; 13 had a mastectomy, 7 had breast-conserving surgery, and for three, the type of surgery could not be verified (Table 2). Eighteen (45.0%) women received systemic therapy (either chemotherapy, tamoxifen, or trastuzumab) during pregnancy (Table 2). Neoadjuvant chemotherapy was given to eight (44.4%), whereas nine (50.0%) received systemic therapy after surgical treatment. For five (12.5%)

TABLE 2 Diagnosis and management of 40 women with gestational breast cancer, Australia and New Zealand, 2013-2014

	Timing of diagnosis				
	1st trimester N = 7	2nd trimester N = 18	3rd trimester N = 15	Total N = 40	P value
Breast symptoms before diagnosis					
Yes	6	14	13	33	.650
No	0	2	0	2	
Not known	1	2	2	5	
Cancer focal					
Unifocal	4	12	7	23	.481
Multifocal	2	3	5	10	
Not known	1	3	3	7	
Surgery during pregnancy					
Yes	7	14	2	23	<.001
No, not recommended	0	0	1	1	
No, delayed until postpartum	0	4	12	16	
Systemic therapy during pregnancy					
Yes	4	14	0	18	<.001
No, not recommended	2	1	2	5	
No, delayed until postpartum	0	3	12	15	
Not known	1	0	1	2	
Timing of delivery					
Preterm	3	9	5	17	.703
Term	4	9	10	23	
Systemic therapy postpartum					
Yes	3	16	10	29	.053
No	3	1	2	6	
Not known	1	1	3	5	

women, chemotherapy was not recommended during pregnancy; four of these had a mastectomy, whereas one, who was diagnosed at 35 weeks' gestation, underwent breast surgery postpartum. Twenty-nine (72.5%) women received systemic therapy postpartum (Table 2).

Of the 25 women diagnosed in the first and second trimesters, 21 (84.0%) underwent surgery, and 18 (72.0%) received systemic therapy during pregnancy (Table 2). No women received systemic therapy in the first trimester. Of the 15 women diagnosed in the third trimester, two (13.3%) who were diagnosed at 28 and 29 weeks' gestation had surgery during pregnancy. No woman diagnosed in the third trimester received systemic therapy while pregnant (Figure 1), but 12 (80.0%) had cancer treatment (surgery and/or systemic therapy) after giving birth.

We observed a difference in management between women diagnosed before and after 30 weeks' gestation. Of the 27 (67.5%) women diagnosed at <30 weeks' gestation, 23 (85.2%) had breast surgery and 18 (66.7%) had systemic therapy during their pregnancy. In contrast, for the

13 (32.5%) women diagnosed at ≥30 weeks' gestation, all breast surgery and systemic therapy were deferred until after birth (see Figure 1).

Data about the use of radiotherapy were available for 37 women. Twenty-three (62.2%) women had radiotherapy, all undertaken postpartum.

3.5 | Labor and birth

Twenty-six (65.0%) women had labor-induced. GBC was recorded as the indication for induction in 21 (80.8%). Of these, nine babies delivered after induction were preterm.

Thirteen (32.5%) women had a cesarean birth, of which nine (69.2%) were without labor. The leading indications for cesarean birth were GBC (30.8%) and fetal distress (30.8%). Seven (53.8%) cesarean births were classified as being performed because of the "urgent threat to the life or health of the woman or fetus" or "maternal or fetal compromise that was not immediately life-threatening."[17]

3.6 | Maternal outcomes

Four (10.0%) women had a postpartum hemorrhage (PPH). One woman with an estimated blood loss of 4000 ml returned to theater for manual removal of placenta, received six units of blood, and was admitted to ICU. This was the only admission to ICU in the study. A second woman with an estimated blood loss of 2100 ml received two units of blood. She had a history of breast-conserving surgery at 25 weeks' gestation followed by adjuvant chemotherapy (doxorubicin and cyclophosphamide) from 29 to 34 weeks before a planned induction of labor. A third woman was induced at 40 weeks and had an estimated blood loss of 1500 ml, whereas a fourth woman had a planned CS at 39 weeks (blood loss of 1350 ml). Neither of these women required a blood transfusion. One woman returned to the theater one day postdelivery and had a laparotomy for exploration of wound before being admitted to a high dependency unit. One woman developed thrombocytopenia. It was unclear from the medical records whether this was secondary to preeclampsia or bone marrow suppression.

There was one late maternal death (>42 days but less than one year after birth) because of metastatic cancer. This woman was diagnosed at 18 weeks' gestation after presenting with a unilateral tender breast lump with warm breast and skin redness over the lump for 3 weeks. Pathology indicated a grade 3 tumor with the maximum tumor diameter of 75 mm. She received neoadjuvant therapy with cyclophosphamide and doxorubicin between 20 and 30 weeks' gestation. Mastectomy was performed at 34 weeks' gestation, and paclitaxel was given postpartum.

3.7 | Last chemotherapeutic dose and birth

Among the 18 women who received systemic therapy during pregnancy, information on the last dose was available for 17. The mean duration between the last dose of chemotherapy and birth was 4.4 weeks (SD 2.8).

3.8 | Neonatal outcomes

There were 40 live-born babies: 27 females and 13 males (Table 3). There were no neonatal deaths or congenital malformations. Ten (25.0%) babies were of low birthweight (<2500 g), and two (5.0%) were small for gestational age.

Seventeen (42.5%) babies were preterm with three moderately preterm (32-33 weeks) and 14 late preterm (34-36 weeks). Sixteen (40%) babies were therapeutic preterm births, and one (2.5%) was a spontaneous preterm birth. Of the 16 therapeutic preterm births, 15 (93.8%) were planned, whereas one involved spontaneous premature rupture of membrane followed by induction of labor. Of the fifteen planned preterm births, the final model of care was recorded for 13. Private obstetrician (specialist) care was the model of care in six (46.2%), high-risk public hospital maternity care in four (30.8%), and public hospital maternity care in three (23.1%). Fourteen (35%) women received corticosteroids for fetal lung maturation, including 12 of the 17 (70.6%) women who had preterm births. Four of the five preterm births without antenatal corticosteroids were inductions (one at 35 and three at 36 weeks' gestation), whereas the fifth birth followed a premature rupture of membranes.

Twelve (30.0%) babies were admitted to a neonatal intensive care unit (NICU) and/or special care unit (SCU); 10 of these were born to women who had received antenatal steroids for fetal lung maturation before birth.

3.9 | Systemic therapy and preterm birth

The rate of preterm birth among women who received systemic therapy during pregnancy was significantly higher than among women who did not (66.7% vs 20.0%, $P < .01$). Of the 12 women who received systemic therapy during pregnancy and had a preterm birth, seven (58.3%) were induced (including one failed induction), one (8.3%) had an unassisted spontaneous vaginal birth, and five (41.7%) had cesarean births. Of the 17 women who had a preterm birth, 15 (88.2%) had systemic therapy postpartum—11 (73.3%) continued systemic therapy initiated antenatally, and four (26.7%) initiated systemic therapy postpartum.

3.10 | Mode of birth and preterm birth

Of the 17 preterm births, 11 (64.7%) occurred after labor induction. Management of GBC was given as the reason for induction in 9 (81.8%) of these women, whereas premature rupture of membrane was indicated in one woman and preeclampsia in the other. Six (35.3%) of the preterm births were CS without labor.

3.11 | Initiation of breastfeeding

Breastfeeding was initiated by 18 (45.0%) women (Table 4), six of whom received systemic therapy during pregnancy. Of these six women, three had a regimen of doxorubicin and cyclophosphamide, two had doxorubicin, cyclophosphamide, and paclitaxel, and one had cyclophosphamide, trastuzumab, and docetaxel. For

TABLE 3 Neonatal outcomes for 40 women with gestational breast cancer, Australia and New Zealand, January 2013-June 2014

Neonatal outcomes[a]	Preterm N = 17	Term N = 23	Total N = 40	P-value
Small for gestational age[b]				
Yes	1	1	2	1.000
No	16	22	38	
Birthweight				
<2500 g	10	0	10	<.001
>2500 g	7	23	30	
Resuscitation required				
Yes	8	2	10	.009
No	9	21	30	
Respiratory support required				
Yes	2	0	2	.162
No	14	23	37	
Not known	1	0	1	
APGAR score (5 min) > 7				
Yes	17 (100)	23	40	NA
No	0	0	0	
Admission to neonatal intensive care unit				
Yes	3	0	3	.069
No	14	23 (100)	37	
Admission to special care unit				
Yes	8	2	10	.009
No	9	21	30	
Breastfeeding initiated				
Yes	5	13	18	.088
No	12	10	22	
Separation status				
Discharged home	15	23	38	.174
Transferred to another health facility	2	0	2	

[a] No neonatal death and no congenital abnormality at birth.

[b] Small for gestational age is defined as a birthweight below the 10th percentile for the gestational age.

four of these women, the date of their last chemotherapy dose was recorded. The median duration between the last chemotherapy dose and date of birth was 48 (IQR, 13.8-59.0) days. At discharge, only three of the six women continued to breastfeed their babies; two women changed to bottle-feeding, and the breastfeeding status for one woman was not recorded.

Of the 29 women who received systemic treatment postpartum, 11 (37.9%) initiated breastfeeding. Five of these women were continuing treatment initiated during pregnancy, whereas six commenced systemic treatment postpartum.

Eight (53.3%) of 15 women who had a mastectomy initiated breastfeeding. Of the seven women with a mastectomy who did not initiate breastfeeding, six either continued their antenatal systemic therapy postpartum or initiated postpartum systemic therapy, and one had a bilateral mastectomy. Seven women had breast-conserving surgery. Three of these initiated breastfeeding, and four did not as they had ongoing management with chemotherapy postpartum and initiation of radiotherapy postpartum.

After discharge, 55.6% of the women who initiated breastfeeding continued to breastfeed their babies, whereas 27.8% used bottle-feeding and 11.1% used expressed breast milk (the type of feeding could not be verified for one woman, 5.6%). Lactation suppression was used among 21 women (52.5%) with postpartum systemic therapy being the main indication for lactation suppression in 18 (85.7%) of these women (Table 4).

TABLE 4 Initiation of breastfeeding of 40 women with gestational breast cancer, Australia and New Zealand, January 2013-June 2014

Management of gestational breast cancer	Breastfeeding initiated	
	Yes (n = 18)	No (n = 22)
Surgery during pregnancy		
Yes	12	11
Breast conservation	3	4
Mastectomy	8	7
Not known	1	0
No, not recommended/ delayed until the end of pregnancy	6	11
Systemic therapy during pregnancy		
Yes	6	12
Neoadjuvant	4	4
Adjuvant	2	7
Not known	0	1
No, not recommended/ delayed until the end of pregnancy	11	9
Not known	1	1
Systemic therapy postpartum		
Yes	11	18
No	4	2
Not known	3	2
Use of lactation suppression		
Yes	3	18
No	14	3
Not known	1	1

4 | DISCUSSION

Reassuringly, our findings revealed no association between management of GBC by antenatal breast surgery and/or systemic therapy (in the second and third trimesters) and congenital anomalies or perinatal death. However, antenatal diagnosis of GBC was associated with very high rates of therapeutic preterm birth (40.0%) with two-thirds of these babies admitted to higher-level neonatal care.

A recent study investigating presenting symptoms of breast cancer in England reported that a breast lump is a presenting symptom in 83% of symptomatic women with breast cancer—76% lump alone; and 7% lump and other symptoms.[18] This finding concurs with our study, where 'breast lump' was the main presenting sign for all 33 women who had symptoms before a confirmed diagnosis of breast cancer. The presence of breast lumps is not uncommon during pregnancy, with approximately 80% of these being benign.[19] Nonetheless, our findings suggest that breast lumps detected during pregnancy should be investigated.[20]

Over 40% of the women with GBC included in this study had a preterm birth. Although this result is marginally lower than rates previously reported in an Italian study (50%) and a retrospective NSW data-linkage study (52%),[9,21] it is more than five times the overall rate of preterm birth in Australia.[22] Our study further revealed that the rate of preterm birth was higher among women who received systemic therapy during pregnancy compared with those who delayed treatment until after birth. This finding, per se, does not suggest the elevated burden of preterm birth seen in GBC is explained by exposure to chemotherapy during pregnancy as two American studies report that women who receive chemotherapy during pregnancy have a similar rate of spontaneous preterm delivery as the general population.[23,24] Rather, our findings suggest that iatrogenic factors, including therapeutic decision-making around when to initiate and cease systemic therapy and timing of birth, may in part explain the very high rate of preterm birth seen in babies of women with GBC.

Relevant guidelines recommend that treating clinicians discuss the timing of birth with women with GBC.[25] Our findings may reflect such practices with 21 of the 26 induced births in our study directly related to cancer management. Nine of these inductions resulted in preterm births ranging from 34 to 36 weeks.

The Royal College of Obstetricians and Gynaecologists recommend that a minimum of 2-3 weeks be required between the last chemotherapeutic dose and birth to recover maternal bone marrow.[25] The mean duration between the last chemotherapy session and birth in our results was 4.4 weeks with only one woman complicated with thrombocytopenia.

Preterm babies are at increased risk of mortality and short-term and long-term complications.[26–33] Unsurprisingly, given the elevated rates of therapeutic and spontaneous preterm birth observed in this study, our findings also show that the rate of neonatal admission to higher care was twice that of newborns Australia-wide (32.5% vs 15.4%).[22] It is important that clinicians consider the likely psychosocial impact for women and their families of caring for a preterm baby while concurrently initiating or continuing cancer treatment[34] and weigh up the preventable deleterious effects of planned preterm birth.

The model of maternity care provided to women with GBC in our study differed from that provided to women in the general population giving birth in Australia. The percentage of women in our study receiving a private obstetric (specialist) model of care at the time of birth

was over eight times higher than that of the overall population (27.5% vs 3.2%).[35] This shift toward the provision of specialist and high-risk care for women in our study reflects the challenges posed by cancer management during pregnancy. Deciding on a treatment plan for GBC requires careful balancing of the benefits of any intervention to treat the mother and any potential risks of such treatment to the developing fetus. Such decision-making requires cross-disciplinary collaboration with the involvement of specialist oncologists and obstetricians.[36,37]

Eighty-two percent of women in our study were diagnosed in the second or third trimester. This is similar to the findings of Loibl et al., where 42% and 40% of patients had their diagnosis of GBC confirmed in the 2nd and 3rd trimester, respectively.[38] Timing of diagnosis likely affects the cross-disciplinary team's decision-making about the management of cancer and pregnancy. In our study, most women diagnosed before 30 weeks had surgery and/or systemic therapy during pregnancy. In contrast, women diagnosed from 30 weeks onward had their treatment delayed until after birth, which then affected their ability to breastfeed and care for the newborn.

Twenty-nine women commenced or continued systemic therapy postdelivery including 11 of 18 women who initiated breastfeeding. The decision to initiate and maintain breastfeeding is complex as it is linked to multiple factors including cultural, socio-economic, educational, previous birthing, and breastfeeding experiences. This decision-making is further complicated when systemic therapy is involved as it raises concerns about exposure and safety of the baby.[39,40] Mastectomy and contralateral prophylactic mastectomy prevent many women from breastfeeding, and this was evident in our study.[41,42] We found half of the 14 women with unilateral mastectomy initiated breastfeeding their babies. Similarly, three of the seven women who had breast-conserving surgery initiated breastfeeding; the four who did not were receiving ongoing systemic therapy and/or commencing radiotherapy.

Limited evidence is available on the effect of systemic therapy on breastfeeding or the appropriate time to initiate breastfeeding after chemotherapy. It has been suggested that women receiving chemotherapy experience difficulties in initiating breastfeeding because of decreased milk production.[43] Our data support this suggestion as only three of the six women who initiated breastfeeding after receiving chemotherapy during their pregnancy continued to breastfeed their babies at discharge. We did not collect postneonatal follow-up data to determine whether breastfeeding after chemotherapy had any adverse impacts. Further research is required to inform guidelines about the appropriate timing of breastfeeding initiation after chemotherapy.

The prospective population-based design with active case finding and the requirement for pathology confirmation of cases is a major strength of this study. Although case identification was prospective, data were collected from medical records leading to instances of missing data for some variables. The scope of the study was limited to women with GBC who gave birth. It excluded women who experienced early pregnancy loss before 20 weeks' gestation resulting in a birth incidence rather than incidence of breast cancer in pregnancy. The data collection period of this study was 2013-2014, and current clinical approaches may differ from those reported here.

4.1 | Conclusions

A painless breast lump was the main presenting symptom for women with GBC in this study. Pregnant women should be encouraged to undertake regular breast self-examination, whereas maternity care practitioners should consider the possibility of a diagnosis of GBC if they discover a breast lump when conducting breast examinations as part of routine antenatal care. To minimize therapeutic preterm birth, a multidisciplinary birth plan needs to be developed to maximize good outcomes for mother and baby. The high level of planned late preterm birth associated with GBC reflects the clinical challenge of cross-disciplinary women-centered care that balances the risks of prematurity and expectant cancer management. Breastfeeding should be supported where clinically possible. Reassuringly, there were no congenital anomalies or perinatal deaths among all 40 newborns, including those born to the 18 women who received antenatal systemic therapy.

ETHICAL APPROVAL

This study received ethics approval from multiple human research ethics committees, including the New South Wales Population and Health Services Research Ethics Committee (HREC/09/CIPHS/21), and other relevant

ethics committees across Australia and the New Zealand Multi-Region Ethics Committee of the Ministry of Health (MEC/09/73/EXP).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Nadom Safi [ORCID] https://orcid.org/0000-0001-8473-0980

REFERENCES

1. Amant F, Han SN, Gziri MM, Vandenbroucke T, Verheecke M, Van Calsteren K. Management of cancer in pregnancy. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(5):741-753.

2. Lee YY, Roberts CL, Dobbins T, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: a population-based linkage study. *BJOG*. 2012;119(13):1572-1582.

3. Rudolph A, Song M, Brook MN, et al. Joint associations of a polygenic risk score and environmental risk factors for breast cancer in the Breast Cancer Association Consortium. *Int J Epidemiol*. 2018;47(2):526-536.

4. Zagouri F, Dimitrakakis C, Marinopoulos S, Tsigginou A, Dimopoulos MA. Cancer in pregnancy: disentangling treatment modalities. *ESMO Open*. 2016;1(3):e000016.

5. Eibye S, Kjaer SK, Mellemkjaer L. Incidence of pregnancy-associated cancer in Denmark, 1977–2006. *Obstet Gynecol*. 2013;122(3):608-617.

6. Stensheim H, Moller B, van Dijk T, Fossa SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. *J Clin Oncol*. 2009;27(1):45-51.

7. Andersson TM-L, Johansson ALV, Hsieh C-C, Cnattingius S, Lambe M. Increasing incidence of pregnancy-associated breast cancer in Sweden. *Obstet Gynecol*. 2009;114(3):568-572.

8. Ives AD, Saunders CM, Semmens JB. The Western Australian gestational breast cancer project: a population-based study of the incidence, management and outcomes. *Breast*. 2005;14(4):276-282.

9. Safi N, Saunders C, Hayen A, et al. Gestational breast cancer in New South Wales: a population-based linkage study of incidence, management, and outcomes. *PLoS One*. 2021;16(1):e0245493.

10. Farquhar CM, Li Z, Lensen S, et al. Incidence, risk factors and perinatal outcomes for placenta accreta in Australia and New Zealand: a case–control study. *BMJ Open*. 2017;7(10):e017713.

11. Sullivan EA, Javid N, Duncombe G, et al. Vasa previa diagnosis, clinical practice, and outcomes in Australia. *Obstet Gynecol*. 2017;130(3):591-598.

12. Donnolley N, Butler-Henderson K, Chapman M, Sullivan E. The development of a classification system for maternity models of care. *Health Inf Manag*. 2016;45(2):64-70.

13. Australian Institute of Health and Welfare. Australia's mothers and babies 2013—in brief. Perinatal statistics series no. 31. Cat no. PER 72. 2015.

14. Australian Institute of Health and Welfare. Australia's mothers and babies 2014—in brief. 2016.

15. PMMRC. Ninth Annual report of the perinatal and maternal mortality review committee: reporting mortality 2013. 2015.

16. PMMRC. Tenth Annual report of the perinatal and maternal mortality review committee: reporting mortality 2014. 2016.

17. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Categorisation of urgency for caesarean section. 2015.

18. Koo MM, von Wagner C, Abel GA, McPhail S, Rubin GP, Lyratzopoulos G. Typical and atypical presenting symptoms of breast cancer and their associations with diagnostic intervals: Evidence from a national audit of cancer diagnosis. *Cancer Epidemiol*. 2017;48:140-146.

19. Langer A, Mohallem M, Berment H, et al. Breast lumps in pregnant women. *Diagn Interv Imaging*. 2015;96(10):1077-1087.

20. Amant F, Loibl S, Neven P, Van Calsteren K. Breast cancer in pregnancy. *Lancet*. 2012;379(9815):570-579.

21. Esposito G, Franchi M, Dalmartello M, et al. Obstetric and neonatal outcomes in women with pregnancy associated cancer: a population-based study in Lombardy, Northern Italy. *BMC Pregnancy Childbirth*. 2021;21(1):31.

22. Hilder L, Zhichao Z, Parker M, Jahan S, Chambers G. *Australia's Mothers And Babies 2012*. AIHW National Perinatal Epidemiology and Statistics Unit; 2014.

23. National Toxicology Program. *NTP Monograph: Developmental Effects and Pregnancy Outcomes Associated With Cancer Chemotherapy Use During Pregnancy*. National Toxicology Program; 2013.

24. Cardonick E, Usmani A, Ghaffar S. Perinatal outcomes of a pregnancy complicated by cancer, including neonatal follow-up after in utero exposure to chemotherapy: results of an international registry. *Am J Clin Oncol*. 2010;33(3):221-228.

25. The Royal College of Obstetricians and Gynaecologists. Pregnancy and Breast Cancer. Green–top Guideline No. 12, United Kingdom. 2011.

26. Machado Junior LC, Passini Junior R, Rodrigues Machado Rosa I. Late prematurity: a systematic review. *J Pediatr (Rio J)*. 2014;90(3):221-231.

27. Brydges CR, Landes JK, Reid CL, Campbell C, French N, Anderson M. Cognitive outcomes in children and adolescents born very preterm: a meta-analysis. *Dev Med Child Neurol*. 2018;60(5):452-468.

28. Stritzke A, Thomas S, Amin H, Fusch C, Lodha A. Renal consequences of preterm birth. *Mol Cell Pediatr*. 2017;4(1):2.

29. Kotecha SJ, Dunstan FD, Kotecha S. Long term respiratory outcomes of late preterm-born infants. *Semin Fetal Neonatal Med*. 2012;17(2):77-81.

30. Greenough A. Long-term respiratory consequences of premature birth at less than 32 weeks of gestation. *Early Hum Dev*. 2013;89:S25-S27.

31. Raju TNK, Buist AS, Blaisdell CJ, Moxey-Mims M, Saigal S. Adults born preterm: a review of general health and system-specific outcomes. *Acta Paediatr*. 2017;106(9):1409-1437.

32. Allotey J, Zamora J, Cheong-See F, et al. Cognitive, motor, behavioural and academic performances of children born preterm: a meta-analysis and systematic review involving 64 061 children. *BJOG*. 2018;125(1):16-25.

33. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, et al. A systematic review of severe morbidity in infants born late preterm. *Am J Obstet Gynecol* 2011;205(4):374.e1-374.e9.

34. Lakshmanan A, Agni M, Lieu T, et al. The impact of preterm birth <37 weeks on parents and families: a cross-sectional study in the 2 years after discharge from the neonatal intensive care unit. *Health Qual Life Outcomes*. 2017;15(1):38.

35. Australian Institute of Health and Welfare. *Maternity Care Classification System: Maternity Model of Care Data Set Specification national pilot report November 2014—National Maternity Data Development Project Stage 2. Cat. no. PER 74.* AIHW; 2016.

36. de Haan J, Verheecke M, Van Calsteren K, et al. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. *Lancet Oncol.* 2018;19(3):337-346.

37. Silverstein J, Post AL, Chien AJ, et al. Multidisciplinary management of cancer during pregnancy. *JCO Oncol Pract.* 2020;16(9):545-557.

38. Loibl S, Han SN, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. *Lancet Oncol.* 2012;13(9):887-896.

39. Dennis C-L. Breastfeeding initiation and duration: a 1990–2000 literature review. *J Obstet Gynecol Neonatal Nurs.* 2002;31(1):12-32.

40. Pistilli B, Bellettini G, Giovannetti E, et al. Chemotherapy, targeted agents, antiemetics and growth-factors in human milk: how should we counsel cancer patients about breastfeeding? *Cancer Treat Rev.* 2013;39(3):207-211.

41. Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. *JAMA Surg.* 2015;150(1):9-16.

42. Wong SM, Freedman RA, Sagara Y, Aydogan F, Barry WT, Golshan M. Growing use of contralateral prophylactic mastectomy despite no improvement in long-term survival for invasive breast cancer. *Ann Surg.* 2017;265(3):581-589.

43. Johnson HM, Mitchell KB. ABM clinical protocol #34: breast cancer and breastfeeding. *Breastfeed Med.* 2020;15(7):429-434.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.