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ORIGINAL ARTICLE

Short cervix and preterm birth in the top end

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Abstract

Background: Reducing rates of preterm birth (PTB) remains a significant challenge. The Northern Territory (NT) records some of the highest rates of PTB in the country, especially in First Nations women. In 2014, a Western Australian (WA) preterm birth prevention initiative involved the implementation of seven key initiatives. One of these was routine mid-trimester cervical length measurement. The initiative successfully reduced PTB rates following its first year of implementation. This was the first successful reduction in PTB, including the earlier gestational ages, across a population.

Aims: To assess the uptake of routine cervical length measurement in the Top End of the NT after the success of the WA PTB prevention initiative and assess if treatment of a short cervix improved PTB rates.

Methods: A retrospective cohort study of all women who received antenatal care and delivered their baby at the NT's only tertiary hospital was performed. Mid-trimester ultrasound scan data were collected from two separate time windows, before and after the implementation of the WA intervention. Treatments and gestational age at birth were recorded.

Results: Adoption of routine screening of cervical length measurement at mid-trimester ultrasound in the NT was successful, increasing from 4 to 88%. Detection rates of short cervix doubled. However, there was no difference to PTB rates despite targeted management.

Conclusion: PTB remains a significant challenge in the NT, especially for First Nations women who are found to have a short cervix more commonly than non-Indigenous women in the Top End.

KEYWORDS

cervical cerclage, cervical length measurement, preterm birth, progesterone, Northern Territory, ultrasound

INTRODUCTION

Preterm birth (PTB), defined as birth before 37 weeks' gestational age, is devastatingly prevalent across the Northern Territory (NT). Most recent national data report that the Australian PTB rate is 8.3% and has remained steady over the past 10 years.[1] However, the PTB rate for the NT exceeds the national average and was reported to be 11.4% in 2020. There are twice as many preterm live babies born to First Nations mothers (16%) than to non-Indigenous mothers (8%) in the NT.[2]

In 2014, a Western Australian PTB prevention initiative known as The Whole Nine Months was launched. This was a state-wide intervention population trial that changed the landscape of screening for and managing risk factors for PTB in Western Australia (WA). It consisted of seven interventions. These included avoidance of elective delivery until at least 38 weeks' gestation; routine measurement of the length of the cervix at all mid-pregnancy ultrasound scans; prescription of natural vaginal progesterone for shortened cervix or history of spontaneous PTB; consideration of cervical cerclage for a very short cervix; promotion of smoking cessation; and the establishment of dedicated PTB prevention clinical service.[3] The initiative was successful in reducing the PTB rate state-wide in the first full year of implementation. The PTB rate across WA fell by 7.6% and in the tertiary level centre by 20%. This was the world's first instance of a population-wide intervention program that successfully reduced PTB. Notably, among First Nations women there was a small, non-significant reduction in the state-wide PTB rate initially, followed by an increase in recent years.[4]

Although there may be controversy around the routine ultrasound assessment of the cervix as a means of defining the risk of PTB in low-risk women,[5] there are also good data showing that therapeutic intervention with progesterone among women with a short cervix may reduce the incidence of PTB.[6]

Acknowledging the lack of conclusive evidence to support universal cervical length screening to predict PTB,[7] RANZCOG currently supports the use of initial transabdominal screening of low-risk women with singleton pregnancies at the mid-trimester scan, with additional transvaginal assessment for those with a short cervical length (<35 mm) or full cervical length unable to be clearly viewed.[8] Based on emerging evidence and RANZCOG's support of progesterone use to reduce PTB, adoption of routine cervical length measurement at mid-trimester ultrasound occurred at NT's single tertiary hospital. Initially this was by request from the referring clinician, but evolved over time, to radiology services ensuring it was a routinely recorded measurement.

The primary aim of this study was to determine whether second trimester cervical length ultrasound screening increased among women who delivered at the tertiary hospital after the implementation of the Whole Nine Months initiative (2013 vs 2018). The secondary aims of the study were to compare the prevalence of short cervix detected; short cervix management with progesterone and/or cervical cerclage and PTB rates before (2013) and after (2018) the Whole Nine Months initiative was introduced.

MATERIALS AND METHODS

Study design and population

This was a retrospective cohort study of all women who received antenatal care, had a second trimester ultrasound and delivered their baby (gestation >20 weeks) at the largest and only tertiary hospital in the NT. Pregnancy and mid-trimester ultrasound scan data were collected from two separate time windows before (from 1 January to 30 June 2013) and after (from 1 January to 30 June 2018) the implementation of the Whole Nine Months intervention. Cervical length measurements were considered valid only for analysis where scans were conducted between 14- and 28-weeks' gestation (inclusive). Screening beyond 24 weeks' GA, although not currently recommended,[5] allowed for inclusion of a number of mothers who were late in receiving a routine morphology ultrasound, which can be common in the NT given geographical challenges. Mothers were included through consecutive pregnancies, but multiple gestation pregnancies were excluded. This study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (reference number 2019-3553).

Data sources and definitions

The cohort was identified via the hospital's electronic medical record database. Data on transvaginal ultrasound, cervical length, medication, management, medical history neonatal outcomes and demographics (including age, Aboriginal and Torres Strait Islander status, place of residence) were extracted for eligible mothers and stored in a secure deidentified study database. All transvaginal ultrasound scans were re-evaluated to confirm cervical length measurement data. Residence was categorised as urban versus rural by address recorded on the electronic health record. The urban category encompassed all mothers residing in Darwin and surrounding suburbs or Alice Springs.

The key outcome measures for these studies were:

(i) A documented mid-term (14–28 weeks' gestation) transvaginal ultrasound with cervical length measurement
(ii) A short cervix (cervical length less than or equal to 25 mm at transvaginal ultrasound)
(iii) Documented progesterone, cerclage or observation only management for short cervix
(iv) PTB defined as a gestation of less than or equal to 37 weeks at delivery

Analysis

Both general descriptive and outcome data were described using proportions, with between-group comparisons assessed for statistical significance using the χ^2 test for proportions and the ranksum (non-parametric) or t-test (normal) for comparison of continuous variables. For the primary analysis, we compared prevalence of mothers who had a transvaginal ultrasound screen with documented cervical length measurement in 2013 versus 2018 overall and stratified by First Nations ethnicity (yes/no). Our secondary analyses compared the between-era proportions of women with short cervix detected; short cervix managed with progesterone and/or cerclage (both stratified by Aboriginal ethnicity); and with PTB based on short cervix detection status.

RESULTS

Overall, there were a total of 2233 pregnancies in the two time periods for the study. Following exclusion of multiple pregnancies, those who birthed at less than 20 weeks' GA, no morphology scan performed or morphology scan performed outside of the desired gestational age window and missing data, Cohort 1 comprised of 807 cases, and Cohort 2 comprised of 863 cases (Fig. 1). First Nations women accounted for 30.1 and 26.4% of cohorts 1 and 2, respectively. Sixteen mothers appeared in both cohorts.

Respectively in 2013 and 2018 (Table 1), 22% versus 18% of women lived remotely. The majority of these were First Nations women (88.6 and 82.7%). Overall, there was a small increase in the maternal age, evidenced by fewer women in the 15–24-year-old age group (27% vs 20%; $P < 0.01$). The median gestational age at ultrasound screening was 20 weeks across both cohorts. Diabetes in pregnancy was common and increased exclusively among non-Indigenous mothers (from 10 to 17%; $P < 0.01$). Rates of pre-eclampsia were low (<4%). Smoking remains a concern for First Nations women, approximately 50% in both cohorts, whereas rates fell from 11 to 7% for non-Indigenous women.

First Nations women experienced a far greater burden of PTB than non-Indigenous women (Table 1). In 2018, the PTB rate for First Nations women was 21%. Despite the burden among First Nations women, the biggest increase between eras was seen in non-Indigenous women (from 4 to 9%) though most of this increase occurred in the lowest risk late preterm category (32–36 weeks).

The routine cervical length screening program was successfully implemented. In 2013, only 4% of women had a recorded cervical length at their mid-trimester ultrasound. In 2018, this increased to 88% ($P < 0.01$), a 22-fold increase. Importantly, the overall rate of short cervix detected doubled from 2% in 2013 to 4% in 2018 ($P < 0.01$; Table 2). First Nations women were substantially overrepresented compared to non-Indigenous women (11% vs 1%). Furthermore, in 2018 the three women with a very short cervical length (<10 mm) were all First Nations women.

Although approximately 50% of women with a short cervix were managed with progesterone in both cohorts (Table 3), cervical cerclage use increased substantially in 2018 (22/33, 67%), often in combination with progesterone (10/33, 30%). Women with a cervical length less than or equal to 25 mm at a mid-trimester ultrasound had a PTB rate of 38 and 48% in 2013 and 2018, respectively, confirming that women with a short cervix are at a significant risk of PTB (Table 4). Reinforcing this point, in 2018, women who did not have a short cervix at ultrasound had a PTB rate of 11%, over four times lower than women with a cervical length <25 mm. Despite increases in routine screening (4–88%), detection (2–4%) and management, PTB rates did not decline between 2013 (9%) and 2018 (12%), rather there was a small increase. Cervical length screening and treatment appeared to make no difference to the prevalence of PTB in this study (Table 1).

DISCUSSION

This cohort study described the rates of cervical length screening, short cervix detection, short cervix management and PTB, before (2013) and after (2018) the implementation of aspects of the Whole Nine Months initiative. Routine cervical length screening was successfully implemented (4–88%), and the enhanced screening doubled the detection and management of women with a short cervix. Short cervix at screening was definitively associated with PTB. First Nations women were 11 times more likely to have a short cervix at routine screening compared to non-Indigenous women. The PTB rate of First Nations women remained high in 2018 (21%) and was 2.4 times higher than that for non-Indigenous women. Unfortunately, our study suggests that the enhanced screening, detection and management did not decrease the PTB rates overall, nor specifically among those with a short cervix. Given the small sample size, it is too early to

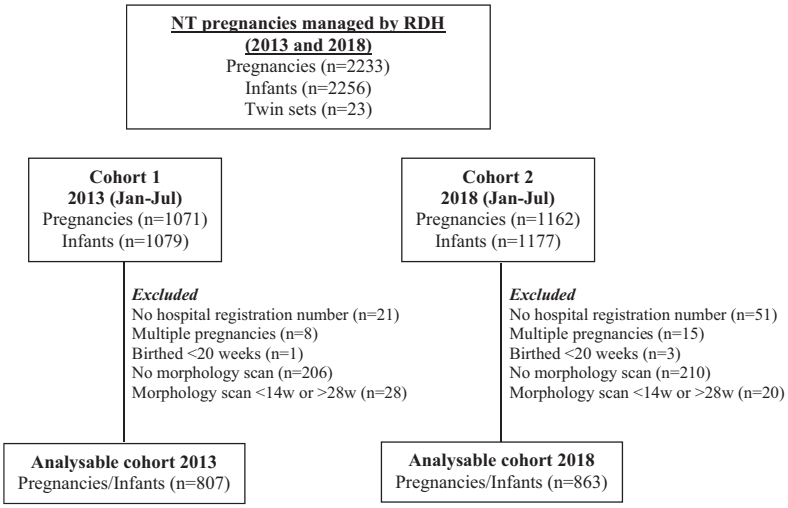

FIGURE 1 Analysable cohort.

TABLE 1 Cohort characteristics: 2013 and 2018

	2013			2018		
	All (*n* = 807)	Aboriginal		All (*n* = 863)	Aboriginal	
		Yes (*n* = 243)	No (*n* = 564)		Yes (*n* = 228)	No (*n* = 635)
Remote dwelling, *n* (%)	176 (22)	156 (64)	20 (4)	156 (18)	129 (57)	27 (4)
Median (range) maternal age in years (at birth)	28 (13-44)	25 (13.43)	29 (16.44)	30 (14.46)	27 (14.43)	31 (18.46)
Maternal age category (at birth), *n* (%)						
0–14	3 (<1)	3 (1)	0 (0)	1(<1)	1 (<1)	0 (0)
15–24	220 (27)	109 (45)	111 (20)	170 (20)	90 (39)	80 (13)
25–34	476 (59)	112 (46)	364 (65)	526 (61)	114 (50)	413 (65)
35–44	108 (13)	19 (8)	89 (16)	164 (19)	23 (10)	141 (22)
44–54	0 (0)	0 (0)	0 (0)	2 (<1)	0 (0)	2 (<1)
Median (range) gestation at morphology screening, weeks	20 (15.28)	20 (16.28)	20 (15.28)	20 (14.28)	20 (14.28)	20 (15.28)
Diabetes in pregnancy, *n* (%)	99 (12)	40 (16)	59 (10)	136 (16)	27 (12)	109 (17)
Pre-eclampsia, *n* (%)	29 (4)	9 (4)	20 (4)	22 (3)	12 (5)	10 (2)
Smoked in pregnancy (>20 weeks' gestation), *n* (%)	151/669 (23)	102/215 (47)	52/447 (11)	128/656 (20)	108/214 (50)	31/461 (7)
Preterm birth (<37 weeks), *n* (%)	69/802 (9)	45/242 (19)	24/560 (4)	104/859 (12)	48/225 (21)	56/634 (9)
Preterm birth category, *n* (%)						
20–27	9/802 (1)	5/242 (2)	4/560 (1)	15/859 (2)	7/225 (3)	8/634 (1)
28–31	5/80 (1)	3/242 (1)	2/560 (<1)	15/859 (2)	8/225 (4)	7/634 (1)
32–36	55/802 (7)	37/242 (15)	18/560 (3)	74/859 (9)	33/225 (15)	41/634 (6)
37–42	733/802 (91)	197/242 (81)	536/560 (96)	755/859 (88)	177/225 (79)	578/634 (91)

TABLE 2 Cervical length screening and short cervix: 2013 and 2018

	2013			2018		
	All (*n* = 807)	Aboriginal		All (*n* = 863)	Aboriginal	
		Yes (*n* = 243)	No (*n* = 564)		Yes (*n* = 228)	No (*n* = 635)
Cervical length screen, *n* (%)	35 (4)	20 (8)	15 (3)	763 (88)	192 (84)	571 (90)
Median (range) cervical length, mm	37 (12.60)	25 (12-60)	40 (13.58)	40 (5.68)	36 (5.60)	40 (11.68)
Short cervix (<25 mm), *n* (%)	13 (2)	11 (5)	2 (<1)	33 (4)	24 (11)	9 (1)
Short cervix (<10 mm), *n* (%)	0 (0)	0 (0)	0 (0)	3 (<1)	3 (1)	0 (0)

make definitive conclusions about whether the program is having a beneficial impact.

The RANZCOG guidelines on routine cervical length measurement suggest that cervical cerclage may be the preferred treatment for an incidental finding of a very short cervix (<10 mm). Routine screening in this study found three women with a very short cervix for which surgical intervention is potentially indicated. Interestingly, cervical cerclage was the most utilised treatment option for all women with short cervices <25 mm. It is important to note that in 2018, vaginal progesterone pessaries were not on

TABLE 3 Management of women with a short cervix (<25 mm): 2013 and 2018

	2013			2018		
	All (*n* = 13)	Aboriginal		All (*n* = 33)	Aboriginal	
		Yes (*n* = 11)	No (*n* = 2)		Yes (*n* = 24)	No (*n* = 9)
Management						
Observation only, *n* (%)	0 (0)	0 (0)	0 (0)	2 (6)	1 (4)	1 (11)
Progesterone only, *n* (%)	5 (38)	5 (45)	0 (0)	7 (21)	6 (25)	1 (11)
Cerclage only, *n* (%)	3 (23)	3 (27)	0 (0)	12 (36)	10 (42)	2 (22)
Both progesterone and cerclage, *n* (%)	2 (15)	1 (9)	1 (50)	10 (30)	7 (29)	3 (33)
Declined, *n* (%)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	1 (11)
None recorded, *n* (%)	3 (23)	2 (18)	1 (50)	1 (3)	0 (0)	1 (11)

TABLE 4 Short cervix detection and preterm birth prevalence: 2013 and 2018

	2013			2018		
	Short cervix			Short cervix		
	Yes (*n* = 13)	No (*n* = 22)	Not screened (*n* = 772)	Yes (*n* = 33)	No (*n* = 730)	Not screened (*n* = 100)
Preterm birth (<37 weeks), *n* (%)	5 (38)	4 (18)	60/767 (8)	16 (48)	77/726 (11)	11 (11)
Preterm birth category, *n* (%)						
20–27	2 (13)	2 (9)	5/767 (1)	4 (12)	9/726 (1)	2 (2)
28–31	1 (8)	1 (5)	3/767 (<1)	2 (6)	10/726 (1)	3 (3)
32–36	2 (15)	1 (5)	52/767 (7)	10 (30)	58/726 (8)	6 (6)
37–42	8 (62)	18 (82)	707/767 (92)	17 (52)	649/726 (89)	89 (89)

the Pharmaceutical Benefits Scheme and could be costly. They were available to women from remote communities at no cost if prescribed by a specialist obstetrician from the tertiary hospital. However, compliance with progesterone pessaries is potentially an issue for women in remote communities. Reasons for this include lack of refrigeration ('Oripro', which was the only available progesterone preparation at the time of the study, needs to be stored in temperatures <25 degrees Celsius[9]) and appropriate storage, and lack of privacy to administer the medication especially where housing overcrowding is common.

Although the pathophysiology of spontaneous cervical shortening is not well understood, there are multiple other well-recognised risk factors associated with PTB. The prevalence of smoking remains a significant challenge for pregnant First Nations women. PTB is significantly more common among First Nations women who smoke[10] and may be the single most important and modifiable driver of the discrepancy in rates of PTB between First Nations and other Australian women. Further, emerging research suggests that at least one quarter of all PTB's, especially those that occur due to spontaneous preterm labour, are attributed to intrauterine bacterial infection, particularly at earlier gestational ages.[11] A dysbiotic vaginal microbiome and the mother's associated inflammatory response have been proposed as an underlying mechanism for PTB.[12] Understanding the difference in the vaginal microbiome taxa in First Nations women and its contribution to PTB is an area for further research.[13] The reason for the shift in prevalence of diabetes in pregnancy between the 2013 and 2018 cohorts remains unclear, but is likely attributed to changes in testing and diagnosis of gestational diabetes that occurred during the time period.[14]

There were some major challenges with data collection. There are multiple electronic record databases used across different regions within the Northern Territory; thus, pregnancy records had to be retrieved from multiple sites. There are also multiple ultrasound service providers, and therefore locating the mid-trimester ultrasound scan was difficult.

Women were considered screened for cervical length measurement if they underwent an ultrasound scan between 14- and 28-weeks' gestational age. It is well understood that cervical length shortens with increasing gestational age and so if more scans were performed at a later gestational age, this could influence the results. We also noted a slight negative correlation between gestational age at screening and cervical length (data not shown). Importantly, the median age at ultrasound was identical

between the 2013 and 2018 cohorts (20 weeks, interquartile range 19–21 weeks).

Overall, the current literature and clinical recommendations support routine cervical length measurement and management of short cervix with vaginal progesterone. This small study suggests that despite the enhanced use of cervical length screening and management, there was little apparent effect on PTB rates, especially for First Nations women. In our routinely screened 2018 cohort, First Nations women were found to have a short cervix at significantly higher rates than other women, but so far, the pathophysiology underlying this risk remains unclear. The crisis of PTB in the Top End is putting strain on our health system, but more importantly, it is severely affecting families and communities. What is now needed are strategies and treatments that are effective in this group.

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