 DOI: 10.1111/j.1479-828X.2012.01426.x

Original Article

Aeromedical transfer of women at risk of preterm delivery in remote and rural Western Australia: Why are there no births in flight?

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Objective: For more than three decades, women at imminent risk of preterm birth (PTB) in Western Australia have been transferred by small aircraft over long distances to the single tertiary level perinatal centre in Perth, with no known case of birth during the flight. We aimed to review recent experience to understand how aircraft travel may delay PTB.

Design and setting: Retrospective observational study of 500 consecutive Royal Flying Doctor Service (RFDS) transfers of women at risk of preterm labour to the tertiary referral centre, from September 2007 to December 31, 2009.

Main outcome measures: In-flight delivery, complications associated with transfer and factors associated with delay in preterm delivery.

Results: There were no in-flight deliveries or serious complications associated with the aeromedical transfer of these patients. In a multivariable Cox proportional hazards regression analysis, clinical factors in the presentation that were associated with a shorter time from landing to subsequent delivery included cervical dilatation ≥ 4 cm, ruptured membranes, gestational age > 32 weeks and nulliparity. The aircraft reaching an ambient altitude > 14,000 feet, or cabin altitude above zero (sea level), was associated with a delay in time from landing to delivery for women who were not in spontaneous preterm labour.

Conclusions: Our findings add to a 30-year experience that women at risk of preterm labour do not deliver during aeromedical transfer. Ambient and cabin altitude of the aircraft were associated with an extension in the time to delivery after arrival. The mechanisms underpinning this effect warrant further investigation.

Key words: preterm labour, preterm birth, air ambulance, transportation of patients, Western Australia.

Introduction

Preterm birth (PTB) is the major problem in human reproduction in our community and remains one of the key unsolved health issues of our time. It is defined as delivery occurring prior to 37 completed weeks of gestation, and in Australia, 20 weeks is used as the lower cut-off to distinguish PTB from a spontaneous abortion. PTB rates are on the rise, reaching 8.2% in Australia in 2008,[1] with a similar trend seen in other developed countries. The burden of PTB is set to increase, with preterm infants being susceptible to a wide range of short- and long-term complications, and PTB being the largest single cause of the world's annual four million neonatal deaths.

Several studies have shown that preterm infants delivered in centres with high-level care and patient numbers have improved outcomes compared with those of outborn status.[2–5] Similarly, antenatal transfer of a woman presenting with symptoms of preterm labour reduces the mortality and morbidity associated with PTB when compared with postnatal transfer of a preterm infant.[6–8] It has long been the practice in rural WA to transfer women presenting with preterm labour to the sole tertiary perinatal centre in the state, King Edward Memorial Hospital (KEMH), resulting in a very high level of perinatal care regionalisation.[9] During the 25-year period from January 1986 to December 2010, the Royal Flying Doctor Service (RFDS) conducted 11,733 obstetric air transfers in WA (Dr. Stephen A. Langford, pers. comm., 2011).

In 1988, we published the results of a study of 99 consecutive aeromedical transfers of women at high risk of PTB, with no case of in-flight birth.[10] Since that time,

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Received 29 September 2011; accepted 7 February 2012.

anecdotal evidence has confirmed that no preterm deliveries have ever occurred mid-flight on a Western Australian RFDS aircraft. This study aimed to review the practice of aeromedical transfer of women at risk of PTB in WA and to generate hypotheses for future investigations in the area of PTB.

Materials and Methods

Five hundred consecutive RFDS transfers of women at risk of PTB to KEMH were reviewed, dating from September 2007 to December 21 2009. Ethics approval was received from the Women and Newborn Health Services Ethics Committee. Cases were identified using the RFDS electronic medical database, using diagnosis codes from transfer records. Transfers included cases of both ruptured and intact membranes, as well as spontaneous preterm labour (defined as regular contractions of at least one in ten minutes accompanied by cervical dilatation or effacement) and threatened preterm labour (defined as irregular contractions or regular contractions without accompanying cervical changes). All cases were between 20^{+0} and 36^{+6} weeks gestational age inclusive.

A chart review of the KEMH medical files was performed, and data collected included maternal demographics and assessment, intrapartum details and neonatal outcomes. Flight data were also extracted from the RFDS electronic aviation data base. Of the 500 transfers reviewed, 22 transfers were excluded from the study for reasons, including miscoding of gestational age >37 weeks ($n = 18$), <20 weeks ($n = 1$) and primary transfer reason for other pregnancy complications and not preterm labour ($n = 3$). A further 39 transfers were not matched at KEMH medical records, or their medical files were missing. Therefore, a total of 439 transfers were included in the analysis, involving 419 women and 459 fetuses (including 33 sets of twins). A total 18 women had more than one transfer over this period, seven of whom were transferred for preterm labour in two separate pregnancies.

Categorical data were summarised using frequency distributions, and continuous data were summarised using medians, inter-quartile ranges (IQR) and ranges. Kaplan–Meier survival estimates and log-rank tests were used to assess potential factors influencing time to delivery. Time was defined as the number of days from landing after flight transfer to delivery, transfer to another institution or discharge. Transfers to other institutions and discharges prior to delivery were censored for analysis. Cox proportional hazards regression modelling was used to investigate the effects of clinical and transfer factors on the time to delivery. These included parity, previous PTB, gestational age, cervical dilatation, preterm rupture of membranes, spontaneous preterm labour, tocolytics, ethnicity, smoking, flight distance travelled, in-flight time, ambient altitude and cabin altitude. These factors were modelled simultaneously, including interactions between clinical factors indicative of imminent delivery and transfer factors. When an interaction was present, the hazard ratios (HR) for all levels of the combined variables were presented. Transfer factors were highly correlated, and this resulted in the construction of separate models to illustrate important predictors. All significant factors were summarised using HR and 95% confidence intervals (CI). SPSS 18.0 statistical software (SPSS Inc, Chicago, IL, USA) was used for data analysis. All hypothesis tests were two-sided, and P-values < 0.05 were considered statistically significant.

Results

Study population

Maternal characteristics by transfer are shown in Table 1. Of the 439 transfers, 232 (53%) resulted in the woman being discharged from KEMH prior to delivery. No deliveries occurred during transfer; however, two babies were delivered prior to transfer at the referring centre.

Transfers

The state of WA divided into its geographic regions and the numbers of transfers from each region are displayed in Figure 1. Fifty cases required two flights to complete

Table 1 Maternal characteristics of study population

	All transfers $N = 439$	
Maternal age at transfer (years)	26	(22–31; 15–43)
Gestational age at transfer (weeks) ($n = 432$)	32	(29–34; 21–37)
ATSI	125	29
Nulliparous	161	37
Smoking during pregnancy		
Nonsmoker	272	66
≤ 10 cigarettes/day	65	16
>10 cigarettes/day	79	19
Previous PTB in parous women ($n = 278$)		
0	164	59
1	72	26
≥ 2	42	15
Reason for referral		
PPROM only	103	24
TPTL only	243	55
TPTL and ROM	47	11
SPTL only	38	9
SPTL and ROM	8	2

Data represent median, Q1–Q3, min–max or *n*%, as appropriate. ATSI, Aboriginal or Torres Strait Islander; PTB, preterm birth; PPROM, preterm prelabour rupture of membranes; SPTL, spontaneous preterm labour (regular contractions at least one every ten minutes with cervical change); TPTL, threatened preterm labour (irregular contractions with or without cervical change).

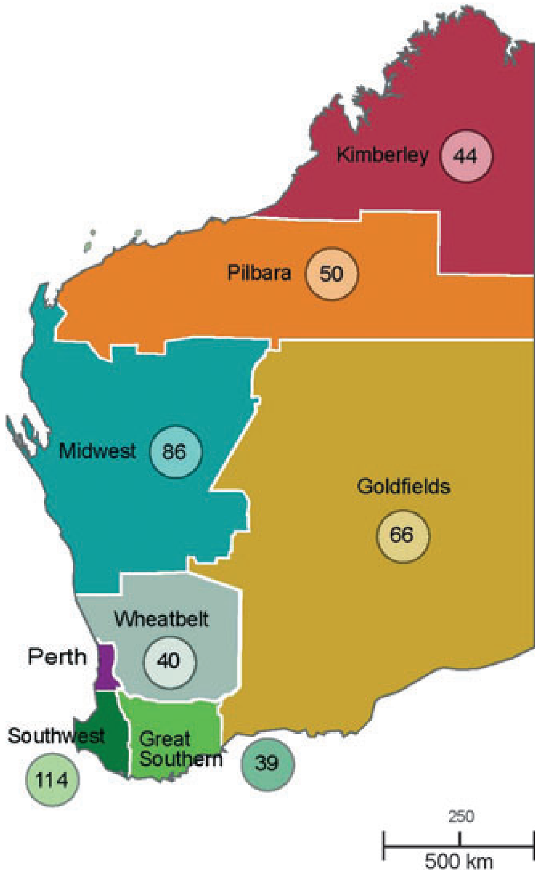

Figure 1 Number of transfers from each geographic region of Western Australia.

the transfer, while seven required three flights, giving 503 transfer legs. The median total transfer time, taken from time of the flight request call to time of landing at Jandakot airport, was 5.5 h (IQR 3.8–8.2 h, range 1.8–40.6 h), and the median total flight time was 76 min (range 30–448 min). The median distance travelled was 393 km (range 131–2811 km), with 102 transfers (23%) of distances >1000 km.

Transfer legs were conducted by single-engine fixed-wing aircraft (n = 323), twin-engine fixed-wing aircraft (n =178) and helicopter (n = 2). The median maximum ambient altitude was 20,000 feet, and the median maximum cabin altitude was 6500 feet. Oxygen administration is included in the RFDS guidelines for emergency obstetric transfers, and the minimum oxygen saturation recorded from pulse oximetry during transfer was 92%. A doctor was required on flight for 78 of the transfers, while a flight nurse staffed the remaining transfers.

Factors influencing time to delivery

Clinical factors significantly associated with a shorter duration of time from landing to delivery in the univariable analysis included spontaneous preterm labour, ruptured membranes, cervical dilatation, gestational age, nulliparity, contraction status and corticosteroid administration (Table 2). Associated transfer factors included flight distance, flight time and maximum ambient altitude. Other demographic and clinical factors considered were Aboriginal or Torres Straight Islander status, smoking status, previous PTB and administration of tocolytics (all P-values >0.05).

Multivariable analysis indicated both ambient altitude and cabin altitude were significantly associated with delivery time for women who were not referred in spontaneous preterm labour (Table 3). The correlation between ambient altitude and cabin altitude was very high (r = 0.93); subsequently, two models were produced to describe the effect of each transfer factor separately.

Model 1 shows women who were not in spontaneous preterm labour at referral, and who travelled at a maximum ambient altitude >14,000 feet, compared with ≤14,000 feet, were more likely to have a delayed time to delivery (HR 0.69, 95% CI 0.50–0.94, P = 0.020) (Fig. 2a). This effect was not found for women in spontaneous preterm labour (P = 0.534), possibly because of the small number of cases in each group (21/44 at altitude ≤14,000 feet).

Model 2 shows women who were not in spontaneous preterm labour at referral, and who travelled at a maximum cabin altitude above sea level, compared with those transferred at a cabin pressure of sea level, were more likely to have a delayed time to delivery (HR 0.66, 95% CI 0.46–0.94, P = 0.022) (Fig. 2b). Because of the small number of women in spontaneous preterm labour travelling at sea level (7/44), further analysis of the effect of cabin altitude on these women was not undertaken.

Clinical factors, including ruptured membranes, cervical dilatation ≥4 cm, gestational age >32 weeks and nulliparity, continued to show significant associations with reduced time to delivery (all P-values ≤0.001). Contraction status, corticosteroid administration, flight time and distance were no longer significant after simultaneous modelling of other factors.

Neonatal outcomes

There were 322 babies, including 28 sets of twins. The median gestational age at birth was 34 weeks (IQR 32–36, range 20.9–41.6), and the median birth weight was 2178 g (IQR 1624–2565, range 260–4795). Two hundred and seventy-nine of the neonates (87%) were delivered preterm, with 238 (74%) >32 weeks gestational age. There were ten stillbirths and six neonatal deaths.

Of the livebirths (n = 312), 34% and 13% of babies had an Apgar score <7 at one and five minutes, respectively. Resuscitation at birth was required for 175 neonates (56%), with 27% of these requiring intubation and ventilation. Median arterial cord blood pH was 7.30, median arterial base excess was −2 mEq/L and median arterial lactate level was 3.4 mmol/L. Intraventricular

Table 2 Unadjusted effect of clinical and transfer factors on time to delivery

	N	Median (IQR) days to delivery		HR 95% CI		*P*-value
Clinical factors						
Parity						
Parous	268	11	2–32	1.00		
Nulliparous	161	3	1–18	1.39	1.10–1.75	0.005
Gestation (weeks)						
≤32	213	14	3–39	1.00		
>32	210	3	1–16	2.08	1.63–2.66	<0.001
PPROM						
Intact	273	17	2–38	1.00		
Ruptured	157	3	1–11	1.78	1.42–2.24	<0.001
SPTL						
No	386	10	2–32	1.00		
Yes	44	1	1–3	3.29	2.35–4.59	<0.001
Cervical dilatation (cm)						
<4	343	10	2–32	1.00		
≥4	26	1	1–2	3.28	2.09–5.16	<0.001
Contractions						
None	76	5	1–16	1.00		
Irregular	147	15	2–39	0.61	0.44–0.84	0.002
Regular	207	4	1–25	0.87	0.65–1.16	0.340
Steroid						
No	114	4	1–22	1.00		
Yes	325	9	2–32	0.71	0.55–0.91	0.008
Transfer factors						
Ambient altitude (feet)						
≤14,000	118	4	1–22	1.00		
>14,000	312	9	2–35	0.68	0.53–0.87	0.003
Cabin altitude						
=Sea level	71	7	1–24	1.00		
>Sea level	359	7	1–31	0.76	0.58–0.99	0.158
Time (h)						
≤1	149	7	1–25	1.00		
>1	281	8	2–32	0.78	0.62–0.98	0.019
Distance (km)						
≤1000	331	6	1–24	1.00		
>1000	99	11	1–38	0.75	0.57–0.99	0.032
Combined factors						
SPTL, ambient altitude (feet)						
No SPTL and ≤14,000	97	11	1–24	1.00		
No SPTL and >14,000	289	10	2–38	0.71	0.54–0.94	0.015
SPTL and ≤14,000	21	1	1–3	2.81	1.66–4.73	<0.001
SPTL and >14,000	23	1	1–3	2.38	1.48–3.82	<0.001
SPTL, cabin altitude						
No SPTL and sea level	64	13	1–25	1.00		
No SPTL and >sea level	322	10	2–35	0.77	0.55–1.06	0.108
SPTL	44	1	1–3	2.63	1.72–4.03	<0.001

Data represents median time from landing to delivery (days), interquartile range (IQR), unadjusted hazard ratio (HR) and 95% confidence intervals (CI). Steroid represents corticosteroid administered previously or during transfer. Ambient and cabin altitudes represent overall maximum altitudes for all legs of the transfer. Flight time and distance represent the overall time and distance taken from commencement to completion over all legs of the flight (recorded by the pilot). Primary reason for transfer: PPROM, preterm prelabour rupture of membranes; SPTL, spontaneous preterm labour.

haemorrhage was documented on cranial ultrasound examination for 25 babies (8%). 132 neonates required a Neonatal Intensive Care Unit (NICU) admission (42%), with a median NICU admission duration of two days (IQR 1–8, range 1–90). The median total duration of stay in a tertiary centre was eight days (IQR 4–21.5, range 0–140).

Table 3 Adjusted effect of factors associated with duration of time from landing to delivery

Factor	HR	95% CI	*P*-value
Model 1			
SPTL, ambient altitude (feet)			
No SPTL and ≤14,000	1.00		
No SPTL and >14,000	0.69	0.50–0.94	0.020
SPTL and ≤14,000	2.29	1.28–4.09	0.005
SPTL and >14,000	2.82	1.68–4.74	<0.001
Parity			
Parous	1.00		
Nulliparous	1.58	1.22–2.04	0.001
Gestational age			
≤32 weeks	1.00		
>32 weeks	2.22	1.69–2.93	<0.001
PPROM			
Intact	1.00		
Ruptured	1.73	1.34–2.23	<0.001
Cervical dilatation			
<4 cm	1.00		
≥4 cm	2.76	1.69–4.50	<0.001
Model 2			
SPTL, cabin altitude			
No SPTL and sea level	1.00		
No SPTL and above sea level	0.66	0.46–0.94	0.022
SPTL	2.41	1.50–3.87	<0.001
Parity			
Parous	1.00		
Nulliparous	1.62	1.25–2.10	<0.001
Gestational age			
≤32 weeks	1.00		
>32 weeks	2.28	1.73–3.00	<0.001
PPROM			
Intact	1.00		
Ruptured	1.80	1.39–2.32	<0.001
Cervical dilatation			
<4 cm	1.00		
≥4 cm	2.77	1.70–4.51	<0.001

Data represents adjusted hazard ratios (HR) and 95% confidence intervals (CI). Primary reason for transfer: SPTL, spontaneous preterm labour; PPROM, preterm prelabour rupture of membranes.

Discussion

Our results show that the aeromedical transfer of women at risk of PTB in WA is safe and, over the study period, did not result in any mid-flight deliveries. In addition, there were no serious complications associated with this practice, in particular relating to the use of salbutamol.

In this study, women not in spontaneous preterm labour who had a transfer exceeding a maximum ambient altitude of 14,000 ft, or a cabin pressure greater than sea level, were significantly more likely to have a longer pregnancy survival time. The ambient altitude is the altitude at which the aircraft is travelling, while the cabin altitude refers to the pressurisation inside the aircraft. Each transfer leg had only one value recorded for maximum ambient altitude and cabin pressure, without details of the duration of time actually spent at these altitudes and pressures. This documentation practice limited our ability to address the relationships between ambient and cabin altitudes and the potential effect on delaying birth after arrival. Further, ambient altitude correlated with flight distance, in such a way that flights of greater distances reached a greater ambient altitude. Distance from the tertiary centre may influence clinical management of a patient presenting at risk of preterm labour and may reduce the threshold for transfer. This was addressed by including flight distance into the multivariate analysis model; however, there may be other factors at play that have not been measured and are not available for consideration. More detailed data on ambient and cabin altitude would be needed to investigate their potential effect on inhibiting preterm labour, and whether a threshold altitude or a dose–response relationship exists. No significant differences were found in women in spontaneous preterm labour, although this may have been limited by small sample size.

As expected, women presenting with ruptured membranes, a cervical dilatation of four or more cm and a gestational age >32 weeks had a shorter median pregnancy survival time when compared with their counterparts. Interestingly, nulliparity was also associated with a shorter median survival time when compared with non-nulliparity. As parous women generally have a shorter duration of labour than nulliparous women, they may be labelled as higher risk, lowering the threshold for transfer. Furthermore, 41% of parous women had a history of previous PTB, an additional risk factor in itself. Therefore, the difference in time to delivery may reflect the use of known risk factors for PTB identified in the history to prioritise antenatal transfers, deeming these women at a greater risk of imminent delivery.

The decision to conduct an obstetric transfer is a judgement by the duty RFDS doctor, in consultation with the referring and receiving doctors, and is based on careful preflight assessment of parity, uterine contractions, cervical dilatation, membrane integrity, fetal heart rate and fetal presentation. It must balance the risk of in-flight delivery with the risk of birth in a less than optimal facility and the implications of subsequent postnatal transfer. Several studies have shown that aeromedical transport of high-risk obstetric patients can be accomplished safely and in a timely manner, even in patients with advanced cervical dilatation,[11–15] although the distances travelled were less than those found in WA.

A substantial proportion (53%) of transfers did not result in delivery at KEMH at the initial admission. The chance of remaining pregnant was found to be related to the reason for transfer, with those presenting with spontaneous preterm labour more likely to deliver in the admission following their transfer, while those transferred because of threatened preterm labour were likely to be discharged undelivered. Similar findings have been observed by others in which 15–40% of women have been shown to leave hospital undelivered or to be still pregnant

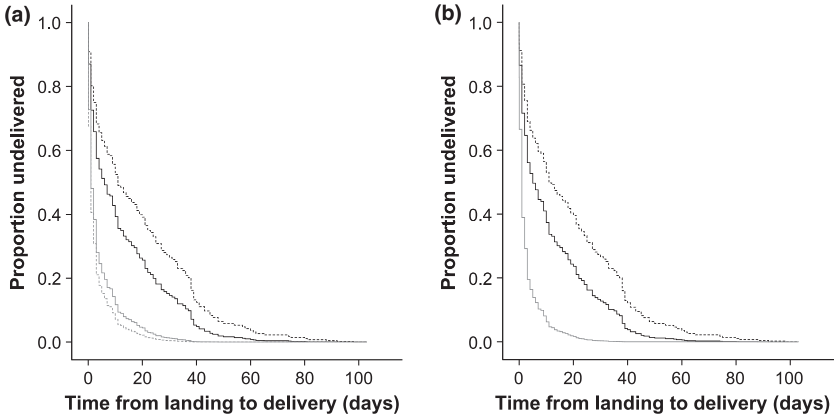

Figure 2 (a) Kaplan–Meier analysis: Proportion of each group remaining pregnant each day after landing. Grey interrupted line: spontaneous preterm labour and ambient altitude >14,000 feet. Grey solid line: spontaneous preterm labour and ambient altitude ≤ 14,000 feet. Black interrupted line: no spontaneous preterm labour and ambient altitude >14,000 feet. Black solid line: no spontaneous preterm labour and ambient altitude ≤ 14,000 feet. Difference between the two black curves is significant (P = 0.020), women in greater altitude group more likely to have a delayed time to delivery. No significant difference between the two grey curves. (b) Kaplan–Meier analysis: Proportion of each group remaining pregnant each day after landing. Grey solid line: spontaneous preterm labour. Black solid line: no spontaneous preterm labour and cabin altitude at sea level. Black interrupted line: no spontaneous preterm labour and cabin altitude greater than sea level. Difference between the two black curves is significant (P = 0.022), women in greater cabin altitude group more likely to have a delayed time to delivery.

one week after transfer.[16] For example, a study in NSW and ACT reported 42% of all preterm transfers discharged undelivered. This was found to be related to the reason for transfer, with preterm contractions alone, as the single most common reason for transfer, associated with the lowest risk of delivery within seven days.[17] In aiming for all preterm deliveries to occur at a tertiary centre, a proportion of cases is inevitably transferred unnecessarily and subsequently discharged undelivered. Antenatal transfers are a portal for rural patients to access specialised obstetric and neonatal care; however, they are nevertheless an expensive intervention. Certainly, current evidence suggests that the interests of the preterm infant are best served by *in utero* transport, rather than postnatal transport of a fragile preterm infant, which, in itself, is also a costly, and arguably more complicated, intervention. The acceptable balance between the two outcomes, the rate of unnecessary antenatal transfers and the rate of postnatal transfers, is not yet defined.

In utero transfer reduces morbidity and mortality associated with PTB, and can be conducted safely, even in a geographic area such as WA. Flying squads consisting of an obstetrician and neonatologist are rarely deployed in WA, and the management of individual cases are based on the observation that in-flight birth is most unlikely. This research supports the RFDS policy of transferring women at risk of PTB in WA and may reassure clinicians of its safety. In addition, preliminary results suggest that ambient and cabin altitudes have an effect on inhibiting preterm labour after arrival.

There has been limited success in the area of PTB prevention, and future research efforts must be innovative. The possible effect of ambient altitude and cabin pressure on delaying preterm delivery and the underpinning mechanism warrant further investigation. More detailed data on the duration of time at altitude are required. Establishing women into clearly identified phenotypes or pathways to PTB would allow better investigation of this relationship. Further, feasible physiological mechanisms need to be identified, for instance the effect of stress hormones and their changing levels during flight, as well as the effect of cabin pressurisation on contractions.

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