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Neurodevelopmental outcome of extremely preterm infants born to rural and urban residents' mothers in Australia

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ABSTRACT

Background: Rural and remote residents in Australia have long experienced unfavourable health outcomes compared to their urban counterparts.
Aims: To study neurodevelopmental outcome at 2–3 years of age, corrected for prematurity of extremely preterm infants admitted to a regional neonatal Australian network from rural and urban regions (based on usual location of maternal residence).
Methods: A multicenter population-based cohort study in which surviving urban and rural infants <29 weeks of gestation born between 1998 and 2004 underwent neurodevelopmental assessment at 2–3 years of age, corrected for prematurity by a developmental assessment team. Moderate/severe functional disability was defined as developmental delay (GQ or MDI > 2 SD below the mean), cerebral palsy (aided for walking), sensorineural or conductive deafness (requiring amplification), and bilateral blindness (visual acuity <6/60 in the better eye).
Results: Of the 1970 infants alive at 2–3 years of age, 268 (63.8%) rural and 1205 (77.7%) urban infants were evaluated. Infants lost to follow-up were of slightly higher gestational age and birth weight. Both rural and urban assessed groups were comparable in gestation and birth weight percentile. In comparison to their urban counterparts, the rural group had more outborn infants (19.8% vs. 4.6%, $p < 0.001$). They, however, did not have an increased risk of moderate/severe functional disability (OR 0.77, 95% CI 0.52–1.23, $p = 0.176$). This finding was not significantly altered by limiting the analysis to different gestational ages.
Conclusion: Extremely premature surviving young children from rural areas of residence do not seem to have an increased risk for moderate/severe functional disability.

1. Introduction

Rural and remote residents in Australia have long experienced unfavourable health outcomes compared to their urban counterparts [1]. Those living in rural and remote areas have a higher prevalence of acute and chronic disease, obesity, low birth weight, hospital admission, adverse health outcomes and decreased life expectancy at birth [2]. Rural areas in Australia encompass vast landscapes with relatively sparse population density. New South Wales (NSW) and the Australian Capital Territory (ACT) cover an area of 815,810 km^2 (10.5% of Australia's total area) and have a total population of 7,588,600 (33% of the total Australian population), with 35% of the population residing in rural and regional areas [3]. Factors that contribute to a rural health disadvantage include geographic isolation and difficulties accessing healthcare, shortage of health services and healthcare providers, including general practitioners and obstetric specialists [4], and a larger Indigenous population who experience substantially poorer health outcomes than non-Indigenous Australians [5].

Due to the lack of specialist obstetric facilities, and the complications associated with preterm birth outside of a tertiary centre [6], it is recommended that mothers at high risk of preterm birth in NSW and ACT be transferred to one of the 10 neonatal intensive care units (NICUs), concentrated in Sydney, Canberra and Newcastle. There are established services for the antenatal transfer of rural mothers requiring tertiary

Abbreviations: CLD, chronic lung disease; FD, functional disability; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; NICU, Neonatal Intensive Care Unit; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; RR, rural residing; UR, urban residing.

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care to urban centres [6], however, the geographical vastness of NSW means that high risk births inevitably occur outside of specialised tertiary centres. The neonatal and paediatric emergency transport service (NETS) in NSW and ACT provides for postnatal transfer of critically ill newborn infants from rural centres to a tertiary hospital that can provide appropriate support [6,7]. There is unequivocal evidence that tertiary centres are best equipped to manage the complications associated with extremely preterm birth [6,8], nevertheless this can be costly for the family and separation from the mother's support network can affect maternal and therefore infant outcomes [8].

We previously reported that the perinatal morbidity of preterm infants born in NSW and ACT did not differ significantly based on rural and urban residence, however mortality was higher in the rural group [9]. Aside from the immediate challenges, however, preterm birth has also been associated with increased risk of long-term neurodevelopmental disabilities compared with term pregnancies, especially if the risk factors and complications at birth are insufficiently managed [10]. Higher rates of cerebral palsy, intellectual disability and sensory impairment, as well as specific learning disability and neuromotor dysfunction have been reported in infants born prematurely [11].

This study aims to compare the neurodevelopmental outcomes at 2–3 years of age of extremely preterm infants born to rural residing (RR) mothers with those of urban residents (UR) in NSW and ACT, Australia. We hypothesise that neurodevelopmental outcomes will be comparable between rural and urban residents.

2. Materials and methods

2.1. Study design and data sources

This study was a retrospective analysis of data extracted from two prospectively collected databases: 1. The Neonatal Intensive Care Units' Data Collection, an ongoing prospective statewide audit of infants admitted to the 10 NICUs in NSW and the ACT during the neonatal period for one of the following reasons: gestational age <32 weeks, birth weight ≤1500 g, assisted ventilation (mechanical ventilation or continuous positive airways pressure), or major surgery (opening of a body cavity). 2. Neonatal Intensive Care Units' follow-up data collection, an ongoing statewide audit at 2–3 years of age, corrected for prematurity, of infants born less than 29 weeks' gestation. A full description of the NICUS and follow-up data and the NSW and ACT neonatal service organization and networking is available elsewhere [6,7].

2.2. Study population and profile of infants who were lost to follow-up

All surviving preterm infants born <29 weeks of gestation and admitted to one of the 10 NICUs in NSW and ACT between 1998 and 2004 who had neurodevelopmental follow-up at 2–3 years of age were included in the study.

Fig. 1 provides the profile of the study group from birth to follow-up among rural and urban residing infants. Of the total 2701 infants with gestational age <29 weeks who were admitted to NICU between 1998 and 2004, approximately 78% were UR and 22% were RR. Of the 2103 infants discharged home after birth, 33 infants died after hospital discharge and 497 infants were lost to follow-up. This left a total of 268 RR and 1205 UR infants on whom assessments were conducted on at 2–3 years of corrected age.

Total of 497 infants were lost to follow-up. A full description of the characteristics of infants who were lost to follow up (n = 497) compared to those who had followed-up assessment (n = 1473) is available elsewhere [12–14]. There were a significant number of RR infants who were lost to follow up (36.2% vs. 22.3%; $p < 0.001$).

2.3. Definitions

The mothers and infants were classified as being rural or urban residents based on the usual residence of the mother at the time of the infant's birth. NSW and the ACT were divided into 16 geographically based local health districts, 8 covering the Sydney metropolitan region, 7 rural and regional NSW and 1 ACT health district. A mother was classified as urban if her usual residence was located in the Sydney Metropolitan, Illawarra, Hunter or ACT health districts as per the reports on NSW health [2] and corresponding with the categories in the accessibility–remoteness index of Australia [15].

2.4. Follow-up assessment

All surviving children were offered a follow-up assessment at age 2–3 years, corrected for prematurity. The majority of children (90.0) were assessed by developmental assessment team at tertiary hospital. If the parents were unable or unwilling to travel to a tertiary hospital, then a local paediatrician or family physician examined the child (10.0%), and the child was referred for detailed developmental assessment service or a tertiary hospital if indicated. Each assessment included examination of hearing, vision, neurological function and developmental assessment using the Griffiths Mental Developmental Scales [16] (GMDS) (85%) or Bayley Scales of Infant Development—II (BSID-II) [17]. The children's heights, weights and head circumferences percentiles were determined, using the NSW population-based birth weight charts at birth and the United States National Center for Health Statistics (NCHS) growth curves at 2–3 years of age, corrected for prematurity. A full description of follow-up assessment is documented elsewhere [12].

2.5. Outcome measures

The primary outcome measure for this study is functional disability (FD) at 2–3 years of age, corrected for prematurity, defined as follows [18]: 1. None/minimal FD: no developmental delay (GMDS-GQ or BSIDII-MDI 1 SD below the mean to 3 SD above the mean); 2. Mild: developmental delay (GMDS-GQ or BSIDII-MDI between 1 and 2 SD below the mean), mild cerebral palsy (able to walk without aids); 3. Moderate: developmental delay (GMDS-GQ or BSIDII-MDI between 2 and 3 SD below the mean), moderate cerebral palsy (able to walk with the assistance of aids), sensorineural or conductive deafness (requiring amplification with bilateral hearing aids or unilateral/bilateral cochlear implant); and 4. Severe: developmental delay (GMDS-GQ or BSIDII-MDI 3 or more SD below the mean), bilateral blindness (visual acuity of <6/60 in the better eye), severe cerebral palsy (unable to walk with the assistance of aids). The diagnosis of cerebral palsy was made if the child had non progressive motor impairment characterised by abnormal muscle tone and a decreased range or decreased control of movements accompanied by neurological signs [19].

Secondary outcome measures included growth at 2–3 years of age corrected for prematurity and short term neonatal outcomes (intraventricular haemorrhage (IVH), chronic lung disease (CLD), retinopathy of prematurity (ROP), necrotising enterocolitis (NEC) and length of NICU stay.

2.6. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (version 20.0; SPSS: SPSS, Inc., an IBM Company, Somers, NY, USA, 2011). Data are presented as number and percentage (%) with odds ratio (OR) and 95% Confidence Interval (CI) or median and interquartile range (IQR). The clinical and demographic characteristics were compared using the Chi-square test with continuity correction and the *t*-test where appropriate.

We also performed stepwise multiple logistic regression elimination analysis to establish independent influence of “urban/rural residence”