J R Coll Physicians Edinb 2008; 38:228–9

CLINICAL

Premature birth: childhood, adulthood and reproduction

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TITLE Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth

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JOURNAL *JAMA* 2008; 299(12):1429–36

DECLARATION OF INTERESTS No conflict of interests declared.

Published online ***August 2008***

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SUMMARY

It is recognised that prematurity is associated with increased short-term mortality and morbidity[1–3] in babies. Swamy and co-workers seek to describe the longer-term outcomes of infants born prematurely. The authors examined survival, reproduction and next-generation preterm birth in babies born in Norway from 1967 to 1988. They used registry data from 1,167,506 singleton births in the Medical Birth Registry of Norway, which is a mandatory registry of all fetal deaths and live births in Norway.

Babies were divided by gender and also into gestation age groups: 22–27 weeks and 28–32 weeks. These groups were then compared in outcomes to singleton term infants (37–42 weeks' gestation). Preterm births are defined as those occurring before 37 completed weeks measured from the first day of mother's last menstrual period. In the Norwegian study this applied to 5.6% of boys and 4.7% of girls.

In the extreme preterm group (22–27 weeks' gestation), there was an increased mortality in early childhood for both boys and girls, and an increased mortality in late childhood for boys. There were no later childhood deaths in girls. Similarly, in the preterm group of 28–32 weeks, the boys had a higher early childhood mortality and late childhood mortality, while girls born in this gestational group showed no evidence of increased mortality.

In adulthood, reproduction was markedly decreased for boys and girls born extremely preterm, and moderately decreased for boys and girls born between 28 and 32 weeks. Women born prematurely were at increased risk of having preterm offspring, but this did not apply to men who had been born prematurely.

OPINION

At the outset, we must commend Norway for having a dataset that is more than 40 years old and that identifies each delivery by a unique eleven-digit number. In the UK, it is hoped that Community Health Index (CHI) numbers will fulfil this task in the near future. This will provide us with a similar opportunity to track such infants reliably, thus providing markedly improved national audit capability.

Much of our understanding of outcomes from extreme prematurity has been gleaned from the EPICure studies (EPICure I and II). The first EPICure study followed babies born in the UK and Ireland at gestation less than 26 weeks during a ten-month period in 1995. This was a prospective study and has provided crucial data on outcomes of neonatal intensive care 13 years ago. Essentially, EPICure I showed:

- 39% survival overall[3]
- Male sex was a risk factor for poor outcome[2]
- Some impairment of motor, visuospatial and sensorimotor function at six years[4,5]
- Poor postnatal growth in the early years of life, especially if chronic lung disease had been treated with prolonged courses of postnatal steroids[2]
- Poor respiratory health over the first six years of life[6]
- Cognitive impairment at eleven years including some language and phonetic difficulties[7]
- 12% had disabling cerebral palsy at six years[4]
- Non-ambulant cerebral palsy was a rare outcome at six and eleven years.[7]

EPICure II[8] involved collecting data for all admissions of fewer than 26 weeks' gestation in England in 2006, using similar methodology to EPICure I. The study group found increased survival in the 952 babies of the 2006 cohort compared with the 1995 cohort, but no clear evidence of a change in early morbidity, such as adverse ultrasound scan of the brain at 36 weeks' gestational age.

It is important that longer-term morbidity is tracked in this new cohort.

There has also been a highly influential study from the US that examined neurodevelopmental impairment at 20 months of age among infants born weighing 500–999 g. Wilson-Costello et al.[9] described the outcomes of 496 such infants born in Ohio between 1982 and 1989, compared with 682 infants born between 1990 and 1998. Survival improved from 49% to 67%. This was, however, achieved with an increased early morbidity rate (including sepsis and chronic lung disease). More worryingly, cerebral palsy rates increased from 16% to 25% and the rate of hearing impairment rose from 3% to 7%. Neurodevelopmental impairment increased from 26% to 36%. In perspective, during the second period, for every 100 infants born, 18 more survived of whom 7 were unimpaired and 11 were impaired.

So what does the Norwegian paper add? This retrospective study provides the most convincing evidence that some adverse outcomes of extreme prematurity may persist into adulthood. Boys in general have a higher absolute mortality rate than their female counterparts, and this may be because of high-risk behaviours or else the higher incidence of congenital abnormalities in boys. It may also be important that congenital abnormalities are more common in preterm babies, thus exaggerating the gender difference.

Equally interesting is the demonstration in this large population that extreme preterm babies, when they reach adulthood, have lower rates of reproduction than term infants at a corresponding age. This intriguing finding may be due to physical factors, but could also be due to psychosocial or economic reasons. In 2001, Phillips et al.[10] showed that low birth weight in men was associated with lower social class, lower income and a lower rate of marriage. Swamy et al. have rightly drawn attention to the fact that they have been assessing in 2004 reproduction rates in adults born between 1967 and 1976: thus their ages at the end of the study were 28 to 37, and one could argue that this cohort may yet have an incomplete reproductive history. Specifically, they could be a group in which some individuals delay having children until later in life.

The authors have further shown that women (but not men) who had been born very prematurely had an increased risk of having a preterm infant. This was 14% of those born at 22–27 weeks, compared with 6.4% of those born at term. It would be fascinating to identify why this is. Could it be that the mothers have inherited either autoimmune disease or pre-eclampsia? These data are unavailable.

One might be forgiven for being discouraged by these data. Nevertheless, there are reasons to be optimistic. The Norwegian data were gathered in infants born between 1967 and 1988 and refer to an era where caesarean section rates were very low, antenatal steroids were used sparingly in Europe and the use of replacement surfactant was in its infancy. These three examples of changes in perinatal practice should make us pause before over-extrapolating to the present day. Furthermore, morbidity does not equate to poor quality of life. An extreme preterm infant may experience chronic lung disease in the early years and yet enjoy a healthy life at school. It is important to recognise that Swamy and co-workers have shown that the majority of extreme preterm babies who live to childhood and adulthood experience good health and can reproduce normally.

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