Preterm birth in rural Malawi – high incidence in ultrasound–dated population.

Chikondi Ntonya[1], Edith Kayira[1], S White[1], George Kafulafula[2], James P Neilson[3], Nynke van den Broek[4].
[1] Malawi–Liverpool–Wellcome Trust Clinical Research Programme
[2] Department of Obstetrics and Gynaecology, College of Medicine, Blantyre
[3] School of Reproductive & Developmental Medicine, University of Liverpool, UK
[4] Liverpool School of Tropical Medicine,

Abstract

Background:
Preterm birth is a major cause of neonatal death, and has an incidence in industrialised countries of 7%. There are still very limited data from developing countries.
Methods:
Cohort study of 512 unselected pregnant women in rural communities in Malawi. All had ultrasound foetal measurements before 24 weeks.
Results:
20.3% of women delivered before 37 completed weeks of pregnancy. Babies born before 37 completed weeks (but after 24 weeks) were more likely to die within the first 24 hours than babies born at term 21.7% vs 3.4% (risk ratio: 6.32, 95%CI 3.21,12.45)
Conclusions:
This population has a very high rate of preterm birth, which is probably infection-related. It may be representative of many rural populations in sub-Saharan Africa. Tackling the problem of neonatal mortality in low income countries will require effective methods to prevent preterm birth.

Introduction

Globally there are an estimated 4 million neonatal deaths (deaths in the first 28 days of life) each year and this accounts for 36% of deaths in children less than 5 years (Lawn et al 2004). The majority (> 75%) of these deaths occur in South Asia and sub-Saharan Africa. The causes of death are poorly documented. In particular, the contribution of preterm birth is unclear. Because of uncertainties about gestational age calculation, low birth weight is often used as a proxy measure for prematurity, but low birth weight can reflect foetal growth restriction, preterm birth, or a combination of both. The incidence of preterm delivery (< 259 days from last menstrual period, equivalent to < 37 completed weeks) is between 5 and 7% in most industrialised countries. There are few reliable data from sub-Saharan Africa.

We have recently completed a randomised controlled trial of vitamin A supplementation to pregnant, anaemic women in a rural area of south Malawi, Namitambo (unpublished). As part of the study protocol, women with singleton pregnancies underwent ultrasound measurements of the foetal biparietal diameter before 24 weeks (mean 20.6 weeks s.d. 3.5). Unexpectedly, we found a high overall incidence of preterm delivery – 24.7% in women with mild anaemia (Hb 8.0-10.9 g/dl) and 29.7% in women with severe anaemia (Hb < 8.0 g/dl).

We are aware of only one other study in Africa using routine ultrasound dating – a study conducted in an urban population in Mozambique (Maputo) reported an incidence of preterm delivery of 15% (Osman et al, 2001) Another study in rural Malawi (Kulmala et al, 2000) described a 22% incidence of preterm delivery in an unselected population but gestational age assessment was based on tape measurement of symphysis-fundal height – a method well recognised as relatively inaccurate in determining gestational age.

If these earlier findings are confirmed, this represents a major, largely unrecognised, public health problem contributing to the high rates of neonatal mortality. In one series from Tanzania, 52% of babies with respiratory distress syndrome (closely associated with prematurity) died (Mlay GS and Manji KP, 2000). An estimate from Malawi suggests that prematurity makes at least as significant a contribution as maternal HIV infection to later, infant mortality (Vaahtera et al, 2000). Our earlier findings were observed in a selected population (women with anaemia) and it is plausible that conditions associated with the anaemia could have contributed to the high rate of prematurity. We have therefore repeated the study in an unselected population of pregnant women.

Methods

Women attending for antenatal care at a health centre (Namitambo) or hospital (Thyolo) were followed throughout their pregnancy and for up to 6 weeks after delivery. Ante- and post- natal care were provided in accordance with the Malawi Ministry of Health Program, which encourages early booking and regular antenatal visits, screening for syphilis and anaemia, provision of antimalarials (sulphadoxine-pyramethamine at 20–24 weeks and 30-34 weeks) and iron supplements, and postnatal visits at week 1 and week 6 post delivery.

95% of women attend for antenatal care in these areas with a mean number of 5.2 (sd 2.6) visits during pregnancy (van den Broek et al, 2003). Antenatal care is generally commenced in this community around 16 - 24 weeks (unpublished information). For this study, consecutive women attending for antenatal care at the health centre and hospital were offered an ultrasound scan at their first antenatal clinic visit (booking) to estimate gestational age if, on abdominal palpation, the uterus seemed to be < 24 week size. Biparietal diameter measurement (Chitty et al, 1994) was performed by specially trained midwives and used to calculate the estimated date of delivery (Concept 2000, Dynamic Imaging). All women with confirmed gestational age less than 24 completed weeks at this first visit were followed prospectively. We documented outcomes including date, type and place of delivery, type of assistance, and condition of mother and baby. For women who delivered in a health facility, birth weight was recorded. Babies were also weighed at the week 1 and week 6 postnatal visits.

Ethical Approval was obtained from the College of Medicine Research Committee, Malawi and permission to work at the Health Centre and Hospital was obtained from the Ministry of Health in Malawi.

Role of the funding source:

Results:

512 women entered the study, 333 from Thyolo and 179 from Namitambo; 33.5 % were primigravid and 17.4% gravida 5 or

more. Mean age was 22.8 years (s.d. 5.6). Just over half of women had skilled assistance at delivery (hospital or health centre 53.2%), 39.2% delivered at home and 7.5% at a traditional birth attendant (TBA) hut. A TBA assisted at 25.6% of all deliveries (at home or in a TBA hut); the grandmother, mother or sister assisted in 16.9% (at home), and in 4% the woman was unattended. Most women had a normal vaginal delivery (93.8%), 4.2% had a caesarean section, 3 women had a ventouse delivery and, for 6 women, the type of delivery was not recorded.

No woman had preterm induction of labour or preterm elective caesarean section. Tocolysis and steroids were not available in any of the health centres and hospitals in this area.

The condition of the baby at birth was available for 456 women (89%). 413 (90.6%) of women reported the baby as being alive after the delivery and in 43 cases (9.4%) the baby was reported dead. Information on gestational age at delivery was available for 453 (88.5%) women. For 11% of women, no date of delivery had been recorded and/or they had moved out of the study area and could not be traced.

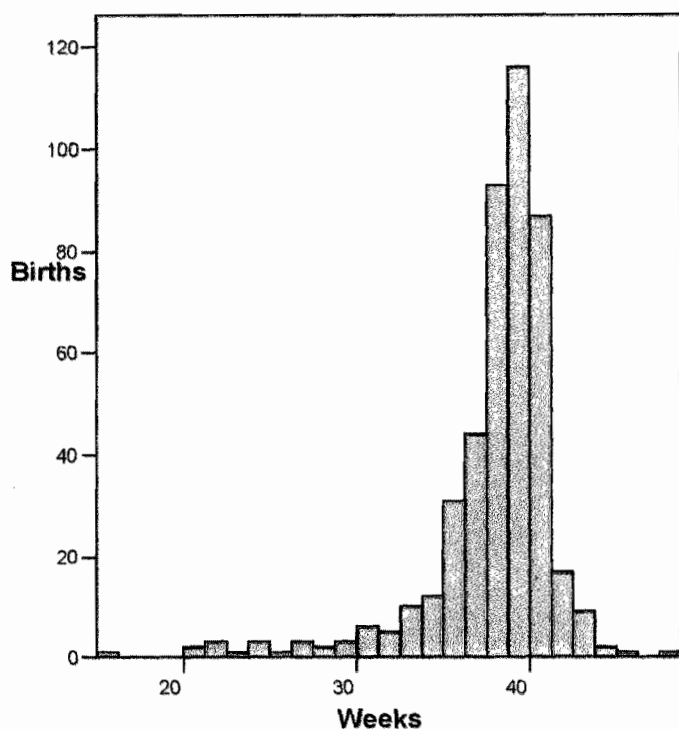**FIGURE 1: Distribution of gestational age at delivery (in weeks)**

Figure 1 gives the distribution of gestational age at delivery. Mean gestational age at delivery was 38.0 weeks, s.d. 3.7.
Preterm delivery (>24 and < 37 completed weeks) occurred in 92 (20.3%) of the 453 women; 72 (16.0%) of these women delivered between 32 and 36 completed weeks, and 20 (4.4%) between 24 and 31 completed weeks.

There was no significant difference in the risk of preterm births for male or female babies. Women who delivered prematurely were more likely to have been unattended or attended by a family member rather than receive skilled attendance at a health centre (risk ratio 1.53, 95%CI 1.03,2.36). Previous preterm labour was reported in 10% of women who delivered between 24 and 32 completed weeks, 6.8% of women who delivered between 33 and 36 weeks and 2.2% of women who delivered after 37 weeks.

TABLE 1: Condition of baby for gestational age at delivery (n= 449)

Gestational age at delivery (weeks)	Number of women	Baby alive	Baby dead
> 37	349	337	12
33- 37	72	67	5
24 -32	20	5	15
< 24	8	0	8
Total	**449**	**40**	**409**

Birth weight was available for 218 babies delivered at the hospital or health centre; 13.3 % had a low birth weight <2500g). Information about both condition of the baby and gestational age at delivery was available for 449 women (87.7%) (**Table 1**)
Babies born before 37 completed weeks (but after 24 weeks) were more likely to die within the first 24 hours than babies born at term 21.7% vs 3.4% (risk ratio: 6.32, 95%CI 3.21,12.45 The mortality was 75% (15/20) for those born after 24 but before 32 completed weeks.

Discussion

This study in an unselected population confirmed our previous observation, in a selected population of women with anaemia during pregnancy, of a high incidence of preterm delivery. These two studies are, to our knowledge, unique in using gestational age assessment based on ultrasound measurement in rural populations in sub-Saharan Africa. Standard biparietal diameter charts have been validated in African populations for gestational age assessment (Munjanja et al, 1988).

There is compelling evidence to link infection with preterm labour (Romero et al, 2004) and this is the probable explanation for the high incidence of prematurity in this population. We have found in previous studies that more than half of the women had high levels of C reactive protein (a marker of infection) during pregnancy (van den Broek and Letsky, 2000), and genital tract colonisation is relatively common (unpublished data). We are currently conducting a randomised trial of antibiotic prophylaxis during pregnancy (APPLe trial) to test the hypothesis that this intervention will reduce the risk of preterm birth.

This population is probably representative of much of rural Africa (van den Broek et al, 2003), which may have similar high levels of infection-related preterm birth. Whether or not ultrasound has any place in clinical obstetric care in low-income countries, it is a vital research tool in future studies of preterm birth. Our findings suggest that prevention of prematurity should be a priority in any attempts to tackle the problem of neonatal mortality in sub-Saharan Africa.
Word count 1,413.

Conflict of interest statement

We declare that we have no conflict of interest.

References
1. Lawn JE, Cousens S, Bhutta ZA, Darmstadt GL, Martines J, Paul V et al. Why are 4 million newborn babies dying each year? *Lancet* 2004; **364**: 399-401.
2. Osman NB, Challis K, Cotiro M, Nordahl G, Bergstrom S. Perinatal outcome in an obstetric cohort of Mozambican women. *J Trop*

Paediatr 2001; **47**: 30-8.

3. Kulmala T, Vaahtera M, Ndekha M, Koivisto AM, Cullinan T, Salin ML et al. The importance of preterm births for peri- and neonatal mortality in rural Malawi. *Paed Perinat Epidemiol* 2000; **14**: 219-26.

4. Mlay GS, Manji KP. Respiratory distress syndrome among neonates admitted at Muhimbili Medical Centre, Dar es Salaam, Tanzania. *J Trop Paediatr* 2000; **46**: 303-7.

5. Vaahtera M, Kulmala T, Ndekha M, Koivisto AM, Cullinan T, Salin ML et al. Antenatal and perinatal predictors of infant mortality in rural Malawi. *Arch Dis Child* 2000; **82**: S200-4.

6. Chitty LS, Altman DG, Henderson A, Campbell S. Charts of fetal size 2: Head measurements. *Br J Obstet Gynaecol* 1994; **101**: 35-43.

7. Munjanja SP, Masona D, Masvikeni S. Fetal biparietal diameter and head circumference measurement – results of a longitudinal study in Zimbabwe. *Int J Gynaecol Obstet* 1988; **26**: 223-8.

8. Romero R, Espinoza J, Mazor M, Chaiworapongsa T. The preterm parturition syndrome. In: Preterm Birth. Eds: Critchley H, Bennett P, Thornton S. 2004. RCOG Press, London.

9. van den Broek NR, Letsky EA. Etiology of anemia in south Malawi. *Am J Clin Nutr* 2000; **72**: S247-56.

10. van den Broek NR, White SA, Ntonya C, Ngwale M, Cullinan TR, Molyneux ME, Neilson JP. Reproductive Health in rural Malawi: a population-based survey. BJOG 2003; **110**: 902-908.