Antenatal and perinatal predictors of infant mortality in rural Malawi

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Abstract

***Background*—The slow pace in the reduction of infant mortality in sub-Saharan Africa has partially been attributed to the epidemic of human immunodeficiency virus (HIV) infection. To facilitate early interventions, antenatal and perinatal predictors of 1st year mortality were identified in a rural community in southern Malawi.**

***Methods*—A cohort of 733 live born infants was studied prospectively from approximately 24 gestation weeks onwards. Univariate analysis was used to determine relative risks for infant mortality after selected antenatal and perinatal exposures. Multivariate modelling was used to control for potential confounders.**

***Findings*—The infant mortality rate was 136 deaths/1000 live births. Among singleton newborns, the strongest antenatal and perinatal predictors of mortality were birth between May and July, maternal primiparity, birth before 38th gestation week, and maternal HIV infection. Theoretically, exposure to these variables accounted for 22%, 22%, 17%, and 15% of the population attributable risk for infant mortality, respectively.**

***Interpretation*—The HIV epidemic was an important but not the main determinant of infant mortality. Interventions targetting the offspring of primiparous women or infants born between May and July or prevention of prematurity would all have considerable impact on infant survival.**

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During the past 30–40 years, childhood mortality rates have declined all over the world. However, this positive development has been slower in sub-Saharan Africa than elsewhere. In this region, appoximately 10% of live born children are estimated to die within their 1st year of life and an additional 7% during the following 4 years. The four million annual deaths for children under 5 years of age in sub-Saharan Africa comprise approximately one third of worldwide mortality in this age group.[1]

Globally, the most common immediate causes for early childhood mortality include infectious conditions such as diarrhoeal diseases, respiratory infections, malaria, and measles.[2] In sub-Saharan Africa and in many developing countries elsewhere, children are especially vulnerable to these diseases, both because of their frequency and widespread malnutrition, and because of a lack of socio-econonomic support for good health.[2–5] As a result, strategies to decrease mortality have included vertical interventions, such as immunisations, other specific preventive measures, and management guidelines for ill children, but also more general approaches such as emphasis on food security and female education.[6]

During the 1980s and 1990s, human immunodeficiency virus (HIV) infection has become increasingly more common among child bearing women in many countries in sub-Saharan Africa.[7–12] Because approximately one third of infected pregnant women pass their infection vertically to their newborn children,[7 13] and mortality among infected infants is very high,[14–16] HIV is likely to have a considerable effect on infant mortality in sub-Saharan Africa. Some authors have even suggested that all recent gains in child survival in this region will be largely or totally offset by the expanding epidemic of HIV.[9 10 15 17 18]

To measure the impact of the HIV epidemic on infant mortality and to compare it with that of other adverse exposures, we conducted a population based, prospective cohort study in rural Malawi. The analysis focused on antenatal, perinatal, environmental, and socioeconomic predictors of mortality—early exposures that predispose the newborns to infant death but do not kill them directly. Immediate causes of death and the impact of postnatal events, such as malnutrition, vaccinations, or changes in family composition, will be reported in a separate communication.

Materials and methods

STUDY AREA

Malawi is a poor southeast African country with approximately 10 million inhabitants. The urbanisation rate is only 14%, and agriculture accounts for over a third of the gross national product, about 90% of export earnings, and 75% of total employment. Crude birth and death rates are 48 births and 22 deaths/1000 inhabitants/year, respectively. The maternal mortality rate is estimated at 620 deaths/100 000 live births, infant mortality rate 135/1000 live born children, and under 5 mortality rate 215 deaths/1000 live born children.[1]

Our study was carried out in Lungwena, an approximately 100 km^2 rural area in southern Malawi. The distance to the nearest town, Mangochi, is 20–40 km. Approximately 17 000 people (mostly islamic) occupy a total of 4200 households in 23 villages. Farming and

fishing form the main occupations, but cultivated land areas are usually too small for adequate food production. Approximately 26% of households possess goats and 35% have chickens that can be sold during the lean season to prevent hunger. Selected household goods, such as bicycles (27%), mattresses (11%), or radios (36%) can be found in the relatively more affluent families. The educational level is very low, with only 14% of pregnant women being able to read and 1% having gone to secondary school.[19] Malaria is endemic throughout the year, with peak prevalences being seen during the rainy season between December and March.

A governmental health centre providing free primary care is located in the middle of the area. The nearest alternative facility offering modern antenatal services is located approximately 15 km away from Lungwena. Because of the distance, this private missionary hospital is virtually inaccessable to the inhabitants of Lungwena, except for those few residing at the southwest end of the area.

PARTICIPANTS AND THEIR BACKGROUND INFORMATION

The details of the recruitment and collection of background data have been described elsewhere.[19] Briefly, all pregnant women presenting for antenatal care between June 1995 and August 1996 were eligible for the study. Before enrolment, informed consent was obtained verbally from each participant. Our study plan was reviewed and approved by the Malawi national health science research committee.

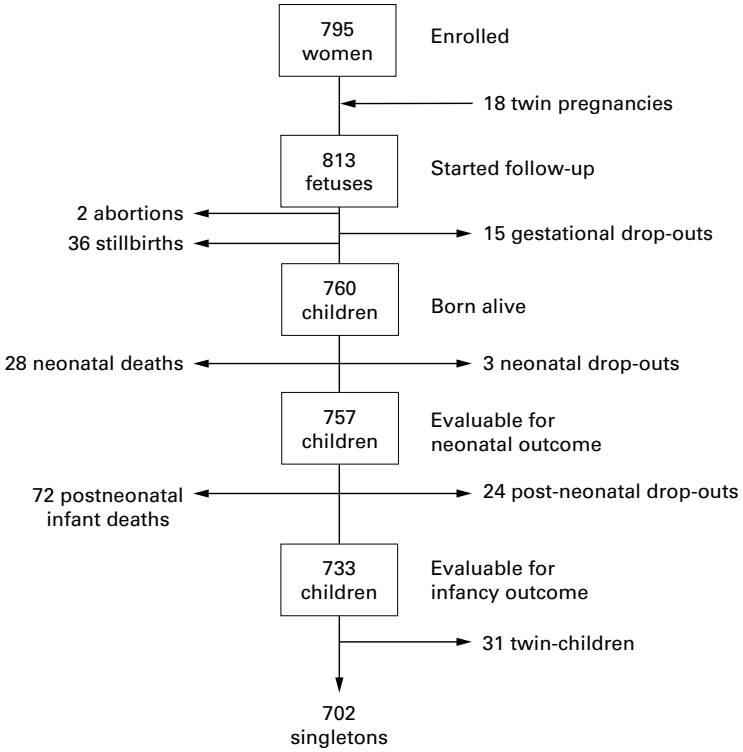

Figure 1 Follow up details of women enrolled in our study.

ANTENATAL FOLLOW UP

The pregnant women were seen at the antenatal clinic of the health centre on average at monthly intervals. At each visit, a nurse/midwife inquired about the participant's recent illnesses, carried out an antenatal examination, and measured her weight and blood pressure with digital instruments accurate to the nearest 100 g and 2 mm Hg, respectively. Obstetric examination included external palpation, auscultation of fetal heart sounds, and measurement of the fundal height with a tape measure. Maternal weekly weight gains were calculated by dividing the total weight gain by the number of weeks in follow up. For women with less than four weeks of follow up, no average gain was recorded.

At the first visit, a 0.1–0.3 ml finger prick capillary blood sample was taken for laboratory analysis. Anti-HIV antibodies were screened from filter paper impregnated blood samples using a standard enzyme linked immunosorbent assay (ELISA) (Genetic Systems LAV EIA; Genetic Systems Corporation, Seattle, USA). Reactive samples were re-tested with another ELISA (Wellcozyme HIV 1+2 GACELISA, VK61; Murex, Dartford, UK). Women whose samples were reactive in both tests were considered to be HIV infected and others uninfected. HIV testing was done with pre-test and post-test counselling, and the result was released in private to those few wishing to know it.

INFORMATION ABOUT THE DELIVERY AND CHILD FOLLOW UP

Approximately 72% of the deliveries took place outside modern health facilities, normally at home under the supervision of a traditional birth attendant. Usually within a week after delivery, a research assistant visited the mother to collect information on the time, place, attendant, duration, and complications of delivery. The newborn weights were measured with spring scales accurate to the nearest 100 g. The first weights were considered birth weights if taken within one week of delivery; otherwise, no birth weight was recorded. Within one month, newborns were examined at the health centre by a member of the research team. Thereafter, a research assistant visited each home monthly to document changes in family composition and to measure the child's growth, morbidity, and mortality. If an infant death was discovered, the assistant reported the death to the research team and a verbal necropsy was carried out.[20]

The length of gestation was estimated by the fundal height at each mother's first antenatal visit. This method was chosen because ultrasound was not available and most women did not remember the dates of their last menstrual period. Dubowitz scoring for maturity was not feasible because most babies were born at home and cultural habits often prevented a home visit during the 1st week of life.

STATISTICAL ANALYSIS

Data entry and analyses were performed using EPI-INFO 6.04b, Microsoft Excel 7.0 and

SPSS 7.5 computer programs. In univariate analyses with dichotomous variables, we calculated relative risks and their 95% confidence intervals and assessed significance with χ^2 tests. For continuous variables, we used univariate logistic regression and the Wald statistic test.

For multivariate modelling of infant mortality, we used logistic regression and exclusion based on likelihood ratio testing. The initial model included those variables that were significantly ($p < 0.05$) associated with mortality in univariate analysis, as well as those known from the literature to be associated with infant mortality. Least significant variables were excluded from the model in a stepwise manner until all remaining variables were significant at $p < 0.1$.

Birth weight was not included in the modelling because it was unknown for many newborns and because of the strong correlation between preterm birth and low birth weight. Maternal weight gain was excluded because several women (especially those with preterm delivery) had insufficient follow up time to determine average weekly gain. Maternal age, education, distance to the health centre, and sizes of cultivated land areas were modelled as linear variables, others as dichotomous variables. Population attributable risks (PAR%) for predictors of mortality were calculated from the adjusted odds ratio (AOR) and appropriate prevalences (p) using the standard mathematical formula:

$$\text{PAR\%} = (\text{AOR} - 1)/(\text{AOR} + (100 - \text{p})/\text{p}) \times 100\%.$$ [21]

Results

STUDY PARTICIPANTS AND THEIR FOLLOW UP

Of the 799 women who started antenatal care at Lungwena Health Centre during the enrolment period, 797 (99.7%) chose to participate in our study. Two of the women were not pregnant and 18 were carrying twins. Thus, a total of 795 women and 813 fetuses were enrolled. A small number (1.9%) of the women discontinued follow up during their pregnancies and 4.7% of fetuses were stillborn. Of the 760 live born children, 733 (96.4%) were available for infancy follow up (fig 1).

Table 1 summarises the relevant background data of those children included in the analysis. There were no differences in the socioeconomic background, maternal health, or newborn findings between the 27 live born infants lost to follow up and the rest of the cohort (data not shown).

Table 1 Background characteristics of 733 study participants

	Value	*n*
Mean area (SD) of cultivated land/household (hectares)	0.6 (0.8)	726
Mean (SD) age of mothers (years)	25.8 (8.9)	732
Proportion (95% CI) of women able to read and write (%)	13.9 (11.5 to 16.6)	732
Proportion (95% CI) of women who were HIV infected (%)	18.5 (15.5 to 21.3)	723
Proportion (95% CI) of primiparous women (%)	23.6 (20.6 to 26.9)	733
Mean (SD) duration of pregnancy at delivery (weeks)	39.4 (2.4)	733
Proportion (95% CI) of preterm (< 38th week) deliveries (%)	20.2 (21.8 to 29.2)	733
Mean (SD) recorded birth weight (g)*	3069 (523)	480
Proportion (95% CI) of low birth weight babies (≤ 2500 g) (%)*	18.3 (15.0 to 22.1)	480

*From infants weighed within the first 7 days of life.
CI, confidence interval; N, number of observations.

Table 2 Infant mortality in a cohort of 733 live born children in Lungwena

	Girls	*Boys*	*Both sexes*
Singletons	118 (41/346)	138 (49/356)	128 (90/702)
Twins	286 (4/14)	353 (6/17)	323 (10/31)
All children	125 (45/360)	147 (55/373)	136 (100/733)

Infant mortality is the number of infant deaths/1000 live born children. The absolute numbers of observed deaths/number of evaluable children are in parentheses.

Active surveillance during and after enrolment identified 37 pregnant women who were not receiving regular antenatal services from the Lungwena Health Centre. Nine of the women had visited the clinic once just before delivery, four had completely missed antenatal care, and five were visitors from other parts of Malawi. Ten women had attended antenatal clinic at the nearby missionary hospital. Thus, 95.2% (795/834) of all pregnant women in the area participated in our study. There were no demographic differences between those women who attended the antenatal clinic at Lungwena Health Centre and those who did not.

MORTALITY

Of the 733 children followed, 100 died during their 1st year of life. Thus, the infant mortality rate was 136 deaths/1000 live born children. Mortality was slightly higher among boys than among girls, and more than twice as common among twin infants than among singletons (table 2). More than a quarter of the deaths occurred during the 1st month of life, but thereafter mortality remained constant. There was no apparent seasonal clustering of infant deaths (data not shown).

DETERMINANTS OF INFANT MORTALITY

Table 3 shows a summary of the variables tested for their association with infant mortality. To facilitate comparison with other studies, analysis was restricted to singleton infants.

In a univariate analysis, maternal primiparity was the strongest predictor of mortality (table 4). Other risk factors included poor maternal

Table 3 Variables analysed as predictors of infant mortality

Maternal and child health
Maternal HIV infection
Mother's parity
Gestational weight gain
Birth before 38th gestational week
Place, attendance, duration, and complications of delivery
Month of birth
Sex of the neonate
First recorded weight
Socioeconomic features
Age of parents
Age of mother at first pregnancy
Age of the previous child at new delivery
Number of previous infant or under 5 deaths in family
Number and age of people in the household
Sex of head of household
Present and former marital status of mother
Size and building material of house
Source of drinking water and presence of a pit latrine at home
Size of cultivated land area
Ownership of domestic animals
Ownership of selected household goods
Distance between home and health centre
Education of parents
Occupation of parents
Religion of parents

Table 4 Factors associated with infant mortality among 702 singleton newborns in Lungwena

Risk factor	*Deaths/total number of children*				
	Exposed	*Unexposed*	*RR*	*95% CI*	*p Value*
Maternal primiparity	37/169	53/533	2.21	5.2 to 18.7	0.000
Birth in May–July	29/129	61/573	2.12	4.2 to 19.5	0.000
First recorded weight < 2500 g	8/39	56/543	1.99	−2.7 to 23.1	0.049
Birth before 38 gestational weeks	30/142	60/560	1.97	3.2 to 17.6	0.001
Maternal HIV infection	26/124	61/568	1.96	2.6 to 17.8	0.002
Christian mother	9/38	81/664	1.94	−2.3 to 25.2	0.039
Female headed family	14/65	63/551	1.89	−0.2 to 20.4	0.020
Maternal weight gain < 200 g/week	40/268	36/392	1.62	0.6 to 10.9	0.023
Maternal education (for each year in school)			1.098	1.001 to 1.204	0.047
Maternal age (for each year)			0.944	0.909 to 0.981	0.003

p Values were tested by means of the χ^2 test.
The exposed group represents those children with the defined risk factor.
The unexposed group represents those children without the defined risk factor.
RR, relative risk; CI, confidence interval.

weight gain, low birth weight, and birth between May and July. Maternal HIV infection, prematurity of child, and young age of mother, as well as some socioeconomic variables, were also associated with infancy deaths (table 4).

In a multivariate analysis controlling for the sex of the child, source of drinking water, sanitation facilities, ownership of domestic animals, presence of fishermen in the household, and all the variables shown in table 4, season of the child's birth was the strongest predictor of infant mortality (adjusted OR, 2.5). Other independent predictors were maternal HIV infection and primiparity, prematurity of child, smaller cultivated land areas, and longer distance to the health centre (table 5). Based on the prevalences and adjusted odds ratios, maternal primiparity accounted for 22%, birth in May to July for 22%, preterm births for 17%, and maternal HIV infection for 15% of the population attributable risk for infant mortality in Lungwena.

When multivariate analysis was restricted to infants surviving the neonatal period, the strongest independent predictors of mortality were birth between May and July (adjusted OR, 2.4), maternal HIV infection (OR, 2.3), and maternal primiparity (OR, 2.3). In contrast, preterm birth was not associated with postneonatal mortality.

Discussion

The aim of our study was to analyse the population level importance of the HIV epidemic and other socioeconomic, maternal, and perinatal determinants of infant mortality in rural Malawi. To avoid selection bias and to allow adjustment for a number of predictors of mortality, we chose a prospective community based cohort approach. The 95% antenatal care enrolment rate, 99.7% recruitment of eligible subjects, and the low drop out rate (1.9% in the perinatal period and 3.6% during the 1st year of life) all made the data representative of the total population of newborns in the study area. The observed infant mortality rate of 136 deaths/1000 live births is comparable with both the national average and mortality rates observed in rural or urban populations elsewhere in Malawi.[1 11 15 16] This suggests that our results might be applicable more widely to rural populations all over the country. However, there are geographical, cultural, and religious differences between various parts of Malawi, so that the widespread applicability of our data remains undetermined.

As early as 1990, vertical HIV infection was suggested to have increased infant mortality rates in some sub-Saharan African countries by 15–26%.[7 14] Subsequent studies, many carried out in Malawi, indicated that children born to HIV positive mothers had at least twofold higher mortality rates than children whose mothers were HIV negative.[11 13 15 16 22 23] Our study of singleton children confirmed this finding and indicated that, on a population level, maternal HIV infections accounted for 15% of all infant deaths, approximately as many as maternal primiparity (22%), births between May and July (22%), and preterm births (17%). Thus, HIV infection was an important, but not the main, determinant of infant mortality in this cohort, despite the almost 20% infection prevalence among the mothers. The importance of the HIV epidemic might increase slightly, but not drastically, in future. This assumption is based on the finding that in urban Malawi HIV seroprevalence among pregnant women has, after a rapid rise, settled at 30–35%.[12] Because only two of the HIV infected mothers died during the child's 1st year, most of the HIV related deaths in our study were likely to have resulted from vertical HIV transmission, rather than suboptimal care of uninfected children.

Maternal primiparity has been noted as a risk factor for infant mortality in earlier cross sectional and cohort studies from developing countries. It has been suggested that part of this effect is attributable to younger maternal age, more frequent maternal infections, and a

Table 5 Adjusted odds ratios for predictors of infant mortality among singleton newborns in Lungwena (n = 664)

	Prevalence	*OR*	*95% CI*	*p Value*	*PAR%*
Birth in May–July	18.4%	2.5	1.5 to 4.2	0.0006	21.6%
Maternal primiparity	24.1%	2.2	1.3 to 3.6	0.0018	22.4%
Birth before 38th gestational week	20.2%	2.0	1.2 to 3.3	0.0119	16.8%
Maternal HIV infection	17.9%	2.0	1.2 to 3.5	0.0083	15.2%
Distance to health centre (for each km)		1.1	1.0 to 1.2	0.0601	
Larger cultivated land area (for each hectare)		0.5	0.3 to 1.0	0.0358	

Results from a logistic regression model including the variables shown in the table as well as maternal age and education as linear variables, complications of delivery (yes/no; includes abnormal presentation of the child, abnormal mode of delivery, or complications to the mother), sex of child (boy/girl), presence of fisherman in the family (yes/no), ownership of domestic animals (yes/no), ownership of pit latrine (yes/no), and source of drinking water (safe/unsafe).
CI, confidence interval; OR, odds ratio; PAR%, population attributable risks.

larger share of preterm deliveries and low birthweight babies among primiparous women.[23–26] In our analysis, primiparity remained an independent and important risk factor even after adjustement for maternal age, the child's prematurity, and numerous socioeconomic variables. A more detailed analysis of the 1st year events will allow an estimation of whether the excess risk for first borns was the result of their low initial weight, a feeding difficulty, failure to thrive, excess morbidity, or suboptimal parental management of sick or malnourished infants.

Preterm birth was the strongest predictor of perinatal and neonatal mortality in our cohort (unpublished data). Although the early deaths of preterm babies accounted for approximately one sixth of all infant deaths in Lungwena, the excess mortality was limited to the neonatal period. Thus, a baby born prematurely but with no additional risk factors in rural Malawi needs no extra surveillance after the first 4 weeks of life. A similar result was found among preterm infants in rural Kenya.[27]

At least one earlier study has documented higher infant mortality among babies born after the rainy season compared with those born during other months of the year.[27] In our study, increased mortality for babies born between May and July was not associated with prematurity or various socioeconomic variables because these were controlled for in the multivariate modelling. The deaths were distributed evenly around the year, ruling out a cohort effect as an explanation. Moreover, average birth weights were highest among infants born between May and July (unpublished data). It is possible that the increased mortality was associated with last trimester adverse exposures (such as more frequent infections) during the rainy season before delivery. However, our data do not provide any means of clarifying the question further.

Taken together, in our cohort of sub-Saharan children, the HIV epidemic had a significant, but not as devastating, effect on infant mortality as has been anticipated.[8–10 28 29] As suggestested earlier, the relative unimportance of HIV was not the result of a low number of HIV related deaths but, rather, the high general mortality in the cohort.[10 18] Therefore, interventions targetting babies born to primiparous women or during a specified season of the year, or those reducing preterm deliveries, are likely to have a major positive effect on infant mortality in sub-Saharan Africa, despite the widespread HIV epidemic. Pragmatic trials are needed to identify the most suitable interventions.

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