Trends and risk factors of stillbirths and neonatal deaths in Eastern Uganda (1982-2011): A cross-sectional, population-based study

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Shortened running title:

Risk factors of stillbirths and neonatal deaths in Uganda

Abstract

Objectives: To identify mortality trends and risk factors associated with stillbirths and neonatal deaths during 1982-2011.

Methods: Population-based cross-sectional study based on reported pregnancy history in Iganga-Mayuge Health and Demographic Surveillance Site (HDSS) in Uganda. A pregnancy history survey was conducted among women aged 15-49 living in the HDSS during May-July 2011 (n = 10,540). Time trends were analysed with cubic splines and linear regression. Potential risk factors were examined with multilevel logistic regression with adjusted odds ratios (AOR) and 95% confidence intervals (CI).

Results: A total of 34,073 births in 1982-2011 were analysed. The annual rate of decrease was 0.9% for stillbirths and 1.8% for neonatal mortality. Stillbirths were associated with several risk factors including multiple births (AOR 2.57, CI 1.66-3.99), previous adverse outcome (AOR 6.16, CI 4.26-8.88) and grand multiparity among 35-49 year olds (AOR 1.97, CI 1.32-2.89). Neonatal deaths were associated with multiple births (AOR 6.16, CI 4.80-7.92) and advanced maternal age linked with parity of 1-4 (AOR 2.34, CI 1.28-4.25) and grand multiparity (AOR 1.44, CI 1.09-1.90). Education, marital status and household wealth were not associated with the outcomes.

Conclusions: The slow decline of mortality rates and easily identifiable risk factors calls for improving quality of care at birth and a rethinking of how to address obstetric risks, potentially a revival of the risk-approach in antenatal care.

Keywords: Epidemiologic Factors; Perinatal Death; Pregnancy; Reproductive History; Stillbirth; Uganda

Introduction

Every year, 2.6 million infants are stillborn[1] and 2.7 million die during their first month of life[2]. An estimated 98-99% of these deaths happen in low- and middle-income countries, where they remain underreported due to a lack of registration systems, births and deaths occurring outside health facilities and cultural beliefs and stigma[3,4].

It is estimated that stillbirth and neonatal mortality rates are highest in sub-Saharan Africa and have decreased at a markedly slower pace in the region compared to the rest of the world[5,6]. Uganda has the fifth highest number of stillbirths and eighth highest number of neonatal deaths in sub-Saharan Africa[6]. Stillbirth rates in the country are based on estimates and predictions with the exception of one study that has investigated stillbirth over time[7]. While a large part of stillbirths and neonatal deaths are caused by potentially preventable diseases or identifiable conditions[8], 50% of stillbirths and 60% of early neonatal deaths have not been linked to any maternal condition[9], highlighting the importance of identifying at-risk pregnancies.

Reviews suggest that stillbirths and neonatal deaths are linked to several biological and socioeconomic risk factors[4,10–12]. While some studies set in sub-Saharan Africa have been published, mostly from Ethiopia[13–18], and Ghana[19–22], a dearth of population-level studies remains. An estimated 57% of deliveries in sub-Saharan Africa take place outside health facilities[23], rendering hospital-based studies unrepresentative. Moreover, findings from settings outside sub-Saharan Africa may not be generalisable due to social, cultural and economic differences. Of the population-based studies on stillbirths in sub-Saharan Africa that we identified[7,11,19,20,24], one examined time trends[7] and one investigated associations with multiple birth, previous stillbirth and infant sex[20], while none of the studies included birth intervals.

The Sustainable Development Goals aim to lower newborn deaths to 12/1,000 live births by 2030, while the Global Every Newborn Action Plan has set a global target of less than 10 stillbirths per 1,000 births by 2035[25]. Achieving these goals is unlikely without significant investments into research providing population estimates and guiding programmatic priorities[5,26]. The objective of this study was to identify risk factors of stillbirths and neonatal deaths in rural Uganda, and to depict the mortality rate trends in 1982-2011.

Methods

Study setting and data collection

The data used in this study were obtained from a cross-sectional survey conducted in order to investigate the reliability of mortality tracking at Iganga-Mayuge Health and Demographic Surveillance Site (HDSS). The site is located in rural Eastern Uganda, covering 65 villages with 16,000 households. The socioeconomic profile of the area is homogenous, with 80% of people earning their living from subsistence farming and retail trading. One hospital, 15 health centres and 24 private clinics serve the 80,000 inhabitants. Nearly 70% of women give birth in a health facility and 30% of women attend four or more antenatal care visits.[27]

The study population consisted of women aged 15-49 living in the HDSS in May–July 2011. We used a list generated from the HDSS database as a guide showing all households in the HDSS and the corresponding females in the household. The data collection team consisted of 60 data collectors working in groups of ten people, visiting all households in the area and identifying and interviewing women aged 15-49. The interviewers asked all respondents what year and month they were born in and then asked for their age in years. The answers were crosschecked and the interviewers attempted to clarify any inconsistencies. If a participant was unsure of her age, the interviewer requested to see documentation containing her date of birth or attempted to estimate the date of birth based on any historical events the respondent was aware of that occurred around the time of her birth.

A maximum of three follow-up visits were made to women who were not home during the first visit. In total, 10,540 women were surveyed (Figure 1; study sample flow chart). During the visit, the data collectors administered a pregnancy history survey. The survey recorded whether a pregnancy resulted in a multiple or a single birth and what the outcome of the pregnancy was (born alive, born dead, miscarriage or induced abortion). Sex of the baby and date of birth was recorded for all pregnancies that did not result in a miscarriage or abortion. If the baby was reported to have been born dead, the mother was asked whether the baby cried, moved or breathed after birth in order to control for misclassification of stillbirths and newborn deaths. Age at death was recorded for babies who were born alive but later died. If the pregnancy ended in a miscarriage or abortion, the month and year of termination of the pregnancy and the duration of the pregnancy were recorded.

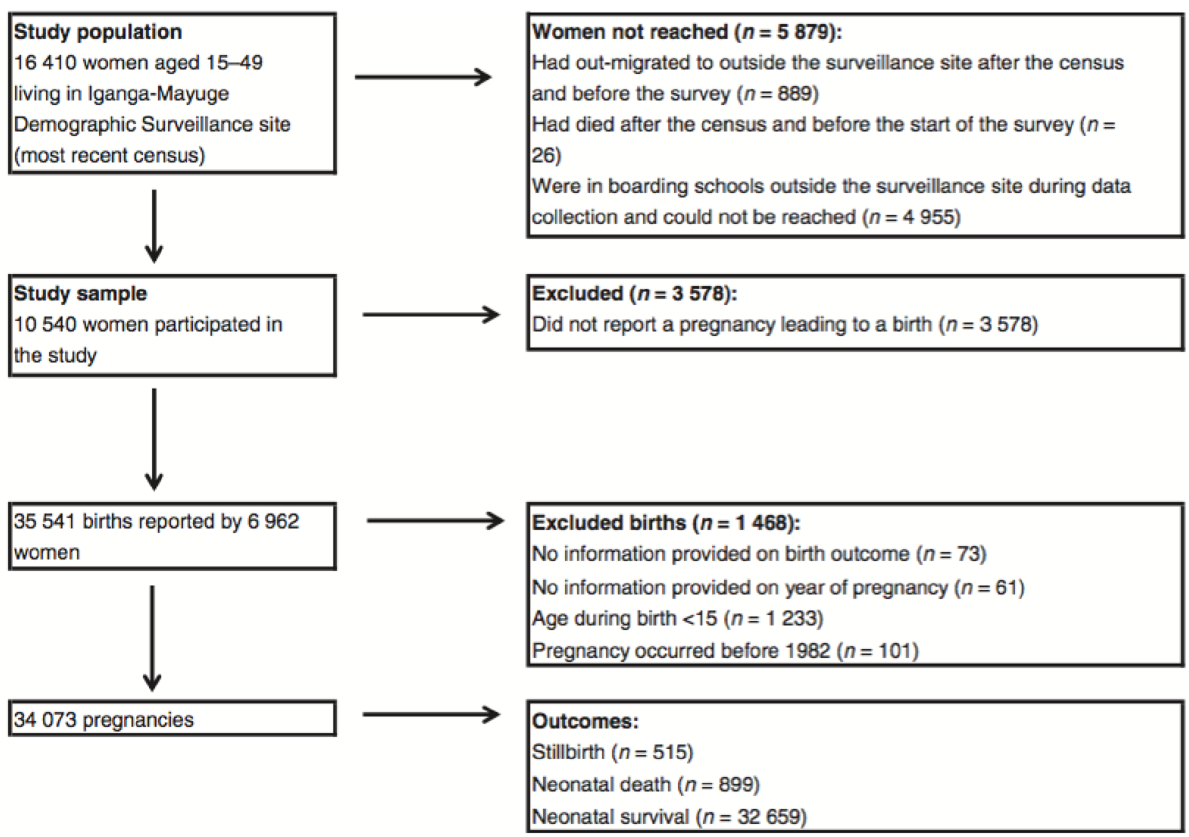

Figure 1 Participant selection flowchart

Variables

The outcome variables were stillbirth, defined as giving birth to an infant who did not move, cry or breathe, and neonatal death, defined as death during the first 28 days of life. We used the thirdtrimester stillbirth definition recommended for international comparison (≥28 weeks of gestation)[28]. We used the year of birth for analysing time trends and as a potential confounder in the analysis for risk factors of stillbirth and neonatal death. Year of birth was treated as a continuous variable in time trend analysis and categorised into six-year intervals for the regression model: 1982-1987, 1988-1993, 1994-1999, 2000-2005, and 2006-2011.

We analysed associations between the outcomes and socioeconomic status, which was reflected by education, marital status and household wealth. The woman's level of education was categorised as none, primary, and secondary or higher. Marital status at the time of the survey was defined as married or single/divorced. The household wealth index was obtained from a separate module and divided into quartiles with ascending household wealth: lowest, second, third and highest. The index was created for an earlier study[29] by doing a principal component analysis (PCA) on variables measuring asset ownership and household characteristics[30]. The approach is often used in settings where it is challenging to obtain reliable estimates of income. The final list included the following variables: number of sleeping rooms, type of floor material, type of roof material, type of wall material, fuel used for cooking, source of light, and the ownership of a radio, a sewing machine, an electric flat iron, type of bed, charcoal flat iron, a bed net, kerosene lamp, kerosene stove, car, tea table, refrigerator, television set, sound stereo, telephone, mattress, wheel barrow, cell phone and camera (Chronbach's alpha = 0.848).

Births were categorised as either single or multiple based on the number of infants born. Sex of the infant was categorised as male, female and unknown. Birth interval was defined as the time between the date of the latest birth and the date of the previous birth, categorised as ≥33 months and <33 months, based on WHO recommendation of a minimum interval of two years between a birth and attempting next pregnancy. Previous adverse outcome was defined as the previous pregnancy resulting in a stillbirth or neonatal death. Age at childbirth was calculated from the dates of birth for the mother and the baby and categorised into 15-17, 18-34, and 35-49 years. Parity was defined as the number of preceding pregnancies leading to a birth after 28 weeks of gestation and categorised as nulliparity, 1-4 births and grand multiparity (≥5 births). In order to investigate whether the association between parity and stillbirth was influenced by maternal age at birth, the variables were combined and births were divided into categories: (1) nulliparous, 15-17 years old; (2) nulliparous, 18-34 years old; (3) parity 1-4, 15-17 years old; (4) parity 1-4, 18-34 years old; (5) parity 1-4, 35-49 years old; (6) parity ≥5, 18-34 years old; (7) parity ≥5, 35-49 years old.

Statistical analysis

We first analysed stillbirth and neonatal mortality rates with chi-square statistics to examine the rates within different levels of the same potential risk factor without adjustment for covariates. Due to the relatively high number of missing values in household wealth (n = 13,745; 40%), we included births with a missing value as a separate group in chi-square analysis. We conducted a univariate logistic regression on the variables that displayed a difference between the outcomes ($p < 0.10$) and included the variables that showed an association in univariate logistic regression in the multivariate model. We constructed a multilevel logistic regression model with odds ratios (OR) and 95% confidence intervals (CI) to identify risk factors of stillbirth and neonatal deaths. The variables in this study were divided into socioeconomic and proximate based on the framework by Mosley and Chen developed to study child mortality in low-income countries[31]. We added socioeconomic variables (education, household wealth, marital status) into the model first and did a backward elimination of variables not reaching p-value of 0.10 or less before adding the proximate variables (age, parity, fetal sex, birth interval, single/multiple birth, previous adverse outcome) and doing another backward elimination. Year of birth was included as a potential confounder in order to control for higher mortality in earlier years. Adjusted odds ratios are only reported for the risk factors that remained significant in the multivariate analysis. We used chi-squares to investigate statistical significance of mortality decline and cubic B-splines to visualise mortality rates with three internal knots at 25th, 50th and 75th percentile for variable year of birth. We obtained the annual decrease in mortality rates with a linear regression on yearly mortality rates that had been transformed into a natural log scale. All analyses were conducted with Stata version 13 (Stata Corporation, College Station, TX, USA).

Ethical considerations

The Higher Degrees, Research and Ethics Committee at Makerere University approved the data collection (ethical clearance: IRB0005876FWA, Protocol 073). Informed consent was obtained from participants in writing or with an inked thumbprint for illiterate individuals after explaining the study verbally and in writing.

Results

The survey intended to interview 16,410 women and 10,540 participated in the study. A large number of women (4,955 women) could not be reached as they were pursuing secondary or tertiary education outside the HDSS; another 889 women had outmigrated and 26 died between survey rounds.

Characteristics of births

All live births and stillbirths during the reproductive age range (15-49) were eligible for inclusion in the analysis (births with maternal age of under 15 were excluded, n = 1,233) . We excluded births from the analysis if information about the year of birth (n = 61) or birth outcome (n = 73) was missing. Births occurring before 1982 (n = 101) were excluded as the low number of observations would have made the mortality rate estimates unreliable. Of the 10,540 women surveyed, 6,962 women reported at least one pregnancy leading to a stillbirth or a live birth and were included in the analyses (Table 1). There were 34,073 reported births in total. Of all births, 515 (1.5%) were reported to have resulted in stillbirth and 899 (2.6%) in neonatal death. The maternal characteristics for most births were primary school education (61.7%), currently married

(88.9%), maternal age 18-34 (80.5%; median 25 years, IQR: 20-30 years) and parity 1-4 (55.3%). Of all infants that were born, 96.7% were singletons, 49.9% were female, 55.3% were linked to a birth interval shorter than 33 months and 2.5% followed a previous birth that resulted in a stillbirth or neonatal death.

Table 1. Characteristics of births at the Iganga-Mayuge Health and Demographic Surveillance Site (N = 34,073)

Item		n	%
Pregnancy outcome	Stillbirth	515	1.5
	Neonatal death	899	2.6
	Live birth	32,659	95.9
Year of pregnancy	1982-1987	2,162	6.4
	1988-1993	4,421	13.0
	1994-1999	7,475	21.9
	2000-2005	9,312	27.3
	2006-2011	10,703	31.4
Education	None	6,358	18.7
	Primary	21,013	61.7
	Secondary and above	6,702	19.7
Household wealth index quartiles	Lowest	3,578	10.5
	Second	5,467	16.0
	Third	6,292	18.5
	Highest	4,991	14.7
	Missing	13,745	40.3
Marital status	Single/divorced	3,741	11.0
	Married	30,300	88.9
	Missing	32	<0.1
Maternal age at childbirth	15-17	3,791	11.1
	18-34	27,438	80.5
	35-49	2,819	8.3
	Missing	25	<0.1
Birth type	Singleton	32,941	96.7
	Multiple	1,120	3.3
	Don't know	6	<0.1
	Missing	6	<0.1
Sex	Female	16,986	49.9
	Male	16,938	49.7
	Don't know	149	<0.5
Birth interval	<33 months	18,829	55.3
	≥33 months	8,029	23.6
Previous adverse outcome	Yes	855	2.5
	No	26,073	76.5
Parity	Nulliparity	6,962	20.4
	1–4 births	18,830	55.3
	Grand multiparity (≥5 births)	8,281	24.3

Time trends in mortality rates

The stillbirth rate and neonatal mortality rate displayed a slow decline (Figure 2). Stillbirths decreased from 20/1,000 births in 1982-1987 (CI 14-26/1,000) to 16/1,000 in 2006-2011 (CI 14-19/1,000) (p = 0.121) (Table S1). There was a statistically significant decline in neonatal deaths (p < 0.001) from 42/1,000 live births in 1982-1987 (CI 22-50/1,000) to 29/1,000 in 2006-2011 (CI 26-32/1,000). The annual rate of change for neonatal mortality was 1.8% per year ($p < 0.01$), while the stillbirth rate decreased by 0.9% per year ($p = 0.19$).

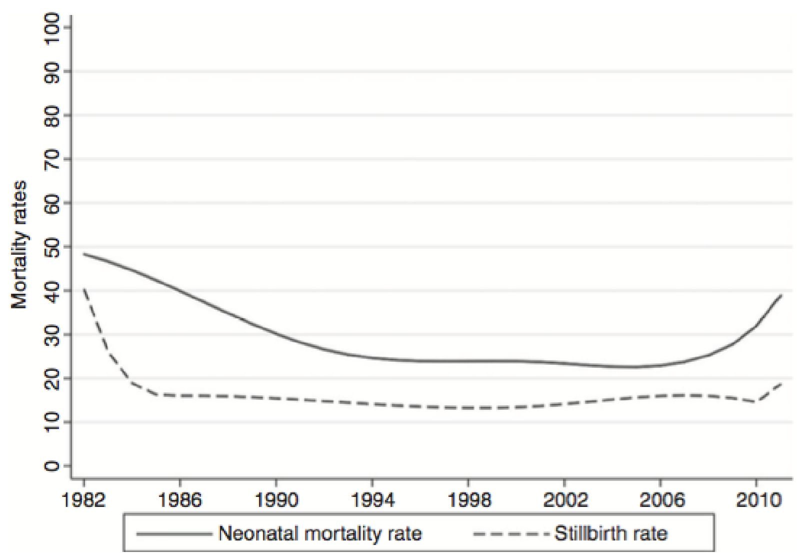

Figure 2 Stillbirth rate (per 1000 total births) and neonatal mortality rate (per 1000 live births) in Iganga-Mayuge Health and Demographic Surveillance Site in rural eastern Uganda from 1982 to 2011.

Table S1. Stillbirth rate (per 1,000 births) and neonatal mortality rate (per 1,000 live births) in Iganga-Mayuge HDSS in 1982-2011 with 95% confidence intervals.

Year	Stillbirths (n)	All births (n)	Stillbirth rate	CI	Neonatal deaths (n)	Live births (n)	Neonatal mortality rate	CI
1982-1987	43	2,162	19.9	14.0-25.8	88	2,119	41.5	22.0-50.0
1988-1993	72	4,421	16.3	12.6-20.0	122	4,349	28.1	23.1-33.0
1994-1999	95	7,475	12.7	10.1-15.2	194	7,380	26.3	22.6-29.9
2000-2005	135	9,312	14.5	12.1-16.9	192	9,177	20.9	18.0-23.9
2006-2011	170	10,703	15.9	13.5-18.6	303	10,533	28.8	25.6-32.0

Risk factors of stillbirth and neonatal death

In the multivariate analysis multiple births carried a 3-fold risk of stillbirth (AOR 2.57, CI 1.66-3.99) (Table 2) and 6-fold risk of neonatal death (AOR 6.16, CI 4.80-7.92) (Table 3) compared to singleton births. The odds of stillbirth were 41% higher for males compared to females (AOR 1.41, CI 1.11-1.80), while male sex was linked to 37% higher odds of neonatal death (AOR 1.37, CI 1.16-1.61). A birth interval of less than 33 months was linked to increased odds of stillbirth (AOR 1.47, CI 1.09-1.98) and neonatal death (AOR 1.50, CI 1.23-1.84). If the previous pregnancy had resulted in a stillbirth or neonatal death, the odds of stillbirth were six times the odds for births not following a stillbirth or neonatal death (AOR 6.16, CI 4.26-8.88), while there was a 4-fold increase in odds for neonatal death (AOR 4.15, CI 3.02-5.72). The combination of advanced maternal age (35-49) and grand multiparity was linked with twice the odds of stillbirth compared to age group 18-35 with a parity of 1-4 (AOR 1.97, CI 1.32-2.89). For neonatal deaths, advanced maternal age was a risk factor for births linked to a parity of 1-4 (AOR 2.34, CI 1.28-4.25) and grand multiparity (AOR 1.44, CI 1.09-1.90).

Table 2. Adjusted and unadjusted odds ratios for stillbirths according to year, socioeconomic and proximate characteristics (n = 34,073 births)

	Stillbirths		All births		Stillbirths per 1,000 births	Unadjusted		Adjusted*	
Independent variables	n	%	n	%		OR	CI (95%)	OR	CI (95%)
Pregnancy year									
1982-1987	43	8	2,162	6	20	1		1	
1988-1993	72	14	4,421	13	16	0.82	0.55-1.23		
1994-1999	95	18	7,475	22	13	0.67	0.45-0.99	0.47	0.27-0.83
2000-2005	135	26	9,312	27	15	0.78	0.54-1.14	0.54	0.31-0.94
2006-2011	170	33	10,703	31	16	0.87	0.60-1.26		
Socioeconomic variables									
Education									
None	84	16	6,358	19	13	0.85	0.61-1.20		
Primary	331	64	21,013	62	16	1.07	0.83-1.39		
Secondary and above	100	19	6,702	20	15	1			
Household wealth index quartile									
Lowest	64	12	3,578	11	18	1.40	0.91-2.15		
Second	86	17	5,467	16	16	1.17	0.79-1.75		
Third	86	17	6,292	18	14	1.04	0.70-1.55		
Highest	63	12	4,991	15	13	1			
Marital status									
Single/divorced	71	14	3,741	11	19	1.35	1.00-1.82		
Married	442	86	30,300	89	15	1			
Proximate variables									
Type of pregnancy									
Single	462	90	32,941	97	14	1		1	
Multiple	49	10	1,120	3	44	3.36	2.37-4.75	2.57	1.66-3.99
Sex of the baby									
Female	182	35	16,986	50	11	1		1	
Male	220	43	16,938	50	13	1.25	1.01-1.53	1.41	1.11-1.80
Birth interval									
≥33 months	96	19	8,029	24	12	1		1	
<33 months	299	58	18,829	55	16	1.35	1.06-1.71	1.47	1.09-1.98
Previous adverse outcome									
No	300	58	25,773	76	12	1		1	
Yes	132	26	855	3	154	6.85	5.06-9.27	6.16	4.26-8.88
Parity and age at birth									
Nulliparous, 15-17 years old	36	7	2,872	8	13	1.15	0.80-1.67		
Nulliparous, 18-34 years old	45	9	4,085	12	11	0.94	0.67-1.32		
Parity 1-4, 15-17 years old	15	3	919	3	16	1.49	0.85-2.62		
Parity 1-4, 18-34 years old	197	38	17,539	51	11	1		1	
Parity 1-4, 35-49 years old	6	1	354	1	17	1.36	0.56-3.32		
Parity ≥ 5, 18-34 years old	152	30	5,814	17	26	2.47	1.97-3.11		
Parity ≥ 5, 35-49 years old	64	12	2,465	7	26	2.35	1.72-3.21	1.97	1.32-2.89

*In the adjusted model, variables were added group by group starting with socioeconomic variables. A backward elimination was performed on all variables not reaching the 0.05 significance level before proximate variables were added in the model. This was again followed by backward elimination. Finally, the year of pregnancy was added in the model. Again, a backward elimination was performed, resulting in the final model.

Table 3. Adjusted and unadjusted odds ratios for neonatal deaths according to year, socioeconomic and proximate characteristics (n = 33,558 births)

	Neonatal deaths		All births		Neonatal deaths per 1,000 live births	Unadjusted		Adjusted*	
Independent variables	n	%	n	%		OR	CI (95%)	OR	CI (95%)
Pregnancy year									
1982-1987	88	10	2,119	6	42	1		1	
1988-1993	122	14	4,349	13	28	0.65	0.48-0.87		
1994-1999	194	22	7,380	22	26	0.61	0.46-0.80	0.47	0.27-0.83
2000-2005	192	21	9,177	27	21	0.48	0.36-0.63	0.54	0.31-0.94
2006-2011	303	34	10,533	31	29	0.67	0.52-0.88		
Socioeconomic variables									
Education									
None	181	20	6,274	19	29	1.29	1.00-1.67		
Primary	562	63	20,682	62	27	1.17	0.95-1.43		
Secondary and above	156	17	6,602	20	24	1			
Household wealth index quartile									
Lowest	93	10	3,514	10	27	1.13	0.82-1.56		
Second	137	15	5,381	16	26	1.07	0.80-1.43		
Third	170	19	6,206	18	27	1.18	0.89-1.56		
Highest	121	13	4,928	15	25	1			
Marital status									
Single/divorced	107	12	3,670	11	29	1.12	0.88-1.42		
Married	792	88	29,858	89	27	1			
Proximate variables									
Type of pregnancy									
Single	757	84	32,479	97	23	1		1	
Multiple	142	16	1,071	3	133	7.64	6.05-9.63	6.16	4.80-7.92
Sex of the baby									
Female	385	43	16,804	50	23	1		1	
Male	502	56	16,718	50	30	1.32	1.15-1.52	1.37	1.16-1.61
Birth interval									
≥33 months	138	15	7,933	24	17	1		1	
<33 months	517	58	18,530	55	28	1.62	1.32-1.97	1.50	1.23-1.84
Previous adverse outcome									
No	560	62	25,773	77	22	1		1	
Yes	108	12	723	2	149	3.99	2.92-5.45	4.15	3.02-5.72
Parity and age at birth									
Nulliparous, 15-17 years old	101	11	2,836	8	36	1.69	1.34-2.13		
Nulliparous, 18-34 years old	116	13	4,040	12	29	1.30	1.05-1.62		
Parity 1-4, 15-17 years old	26	3	904	3	29	1.27	0.83-1.95		
Parity 1-4, 18-34 years old	390	43	17,342	52	23	1		1	
Parity 1-4, 35-49 years old	15	2	348	1	43	2.16	1.22-3.83	2.34	1.28-4.25
Parity ≥ 5, 18-34 years old	169	19	5,662	17	30	1.28	1.06-1.56		
Parity ≥ 5, 35-49 years old	82	9	2,401	7	34	1.57	1.21-2.03	1.44	1.09-1.90

*In the adjusted model, variables were added group by group starting with socioeconomic variables. A backward elimination was performed on all variables not reaching the 0.05 significance level before proximate variables were added in the model. This was again followed by backward elimination. Finally, the year of pregnancy was added in the model. Again, a backward elimination was performed, resulting in the final model.

Discussion

During 1982-2011, neonatal mortality rate decreased by 1.8% and stillbirth rate by 0.9% per year. The odds of stillbirth and neonatal death were higher with a multiple pregnancy, male infant, short birth interval and previous adverse outcome. Neonatal deaths were linked to advanced maternal age and stillbirths were linked to grand multiparity during advanced maternal age. We detected no association with socioeconomic variables.

Earlier studies have reported a similar risk from multiple births[20,32,33] and male fetal sex[12,20,34]. Male sex is a risk factor for neonatal deaths[35,36] and it has been suggested that male fetuses are also more vulnerable to stressors in utero[12]. The association between neonatal deaths and birth intervals shorter than 33 months has been reported in earlier studies[37]. However, few studies have investigated birth intervals and stillbirths exclusively. Our findings are similar to the two studies we were able to identify, which reported an association between risk of stillbirth and birth intervals of less than 21 months[38] and less than 35 months[39]. The association in this study was controlled for previous stillbirth, suggesting that the association is not only linked to maternal characteristics that may result in consecutive stillbirths. The underlying mechanism of action is unclear, but it may be linked to depletion of reproductive and nutritional resources due to physical strain from short birth intervals[37,40,41].

The odds of stillbirth and neonatal death were higher if the previous pregnancy ended in an adverse outcome, consistent with previous studies[20,32,39,42–46]. A recent meta-analysis on studies conducted in high-income countries reported an increased risk of subsequent stillbirth if the initial pregnancy resulted in stillbirth, but pointed out that the association is less clear when the initial stillbirth is unexplained[47]. In addition to being physiological, the association may also be a proxy for either environmental or socioeconomic factors that have not been fully accounted for.

Nulliparity or grand multiparity alone were not associated with stillbirths in this study, in line with findings from Bangladesh[43] and Egypt[48], but in contrast with other studies[7,11,19,46,49]. However, the odds of stillbirth were higher for grand multiparous women with advanced maternal age, similar to findings from other studies[10,11,20,24]. Advanced maternal age is a well-established risk factor for stillbirths[10,11] and it is linked with a higher prevalence of chronic hypertension and placental pathologies[50]. Advanced maternal age was a risk factor for neonatal deaths regardless of parity, consistent with some previous findings[32,51–53] but in contrast to several others[14,21,36,54,55]. The association may be due to age-related birth complications resulting in early neonatal deaths, or less health-seeking behaviour and more observance of potentially harmful traditions among older generations.

While many studies have linked socioeconomic status with stillbirths and neonatal mortality[13,36,46,51,56–59], our findings mirror several other studies that did not find an association with education[19,20,24,32,43,48,49,60], household wealth[19,24,56,60] or marital status[10,24,60]. Socioeconomic factors may have less influence in rural areas, where wealthier and more educated women still face inadequate quality and availability of health services. Moreover, survival around the time of birth is reliant on the availability of medical interventions such as induction and surveillance of labour, assisted vaginal delivery and caesarean section. The findings of this study may be generalisable to women aged 15-49 living in other rural areas in Sub-Saharan Africa, as the socioeconomic and biological risk profile is similar to many other low-resource settings. In urban areas, where there is generally more accessible and better quality health care, socioeconomic factors might exert a larger influence.

To the best of our knowledge, this is one of the first population-based studies that examined time trends and risk factors of stillbirths in sub-Saharan Africa. This study is also among the first studies that use complete pregnancy histories rather than birth histories. The annual rates of change obtained through this method are similar to global estimates overlapping the time period in this paper: 0.9% for stillbirths compared to a global estimate of 1.1% for 1995-2009[61], and 1.8% for neonatal mortality compared to 2% globally for 1990-2012[6], indicating that pregnancy histories are a relatively reliable data collection method. The use of pregnancy histories is in line with the Every Newborn Action Plan, which advocates for more comprehensive pregnancy and newborn data collection in communities while routine data collection systems are being strengthened[25].

This study has some limitations. Education level, marital status and household wealth reflect the situation at the time of the survey. This may have resulted in some pregnancies to be linked to incorrect socioeconomic variables and attenuated the associations, even though very similar results were obtained when the analysis was restricted to births during 2006-2011 (data not shown). Up to 40% of births were to households that did not have household wealth status, probably due to missing asset data from the earlier survey. Moreover, the population in the area is relatively homogenous, which may have diluted the associations. We missed 4,955 women for interview who were schooling outside the study area and could not be reached for interview; most of them in the age bracket 15-17 years. However, few births are likely to have been missed because of this due to the prevailing practice of schools expelling pregnant girls.

Residual confounding is most likely present due to lack of information on antenatal care attendance, place of delivery, maternal conditions and pregnancy complications. We did not have information on pregnancies linked to maternal deaths. Pregnancies with advanced maternal age are underrepresented in earlier years due to the retrospective nature of the survey. These factors may have resulted in underestimated mortality rates. The apparent rise in mortality rates over the more recent years may reflect recall bias, with women more likely to report more recent stillbirths and neonatal deaths. Relying on mothers' recollection of the month and year of termination of pregnancy or neonatal death is also subject to recall bias, which may have led to a non-differential misclassification between miscarriages, stillbirths and neonatal deaths.

The stillbirth rate/neonatal mortality rate ratio was 0.58 in this study, which is in line with population-based retrospective surveys (mean ratio 0.6), but lower than high-quality civil registration and vital statistics data (mean ratio 1.03)[5]. However, in the absence of high quality facility-level data, pregnancy history surveys offer a viable option in resource-poor settings compared to more costly routine surveillance.

The apparent slow rate of decline for both neonatal mortality and stillbirths, lack of association with education and household wealth and the existence of easily identifiable risk factors call for a rethinking on how to address obstetric risks. The risk approach in antenatal care was criticised in the early 2000s and replaced by the statement that every pregnancy is at risk[63]. In response, all mothers are today advised to deliver with a skilled attendant and in a facility. However, our study indicates that multiple pregnancies and pregnancies linked to previous birth complications, grand multiparity and advanced maternal age bear a much greater risk for the baby. A re-positioning of the risk approach with the aim to refer higher risk pregnancies to fully equipped hospitals should be considered. In high income settings around 60% of multiple pregnancies are delivered by Caesarean section[64] while in low-income settings this rate remains below 40% at hospital-level[65]. The re-vitalisation of family planning programmes after a decade of neglect will hopefully also contribute to a decrease of unwanted pregnancies that pose higher risks for the neonate.

Conclusion

This is one of the first population-based studies from Sub-Saharan Africa that investigated trends and risk factors of pregnancy outcomes by using a pregnancy history survey. Based on modelling, the data compared favourably to international estimates. In light of the findings, we encourage improved access and quality of care at birth, an increased focus in targeting high-risk pregnancies during antenatal care and further validation of pregnancy history data.

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Disclosure of Interests

The authors declare no conflicts of interest.

Contribution to Authorship

SK with support from CH and PW conceptualised the study, wrote the initial and the final paper draft and conduced all statistical analyses. DK, JA and GP participated in the initial study design, data collection and management and reviewed and provided input to the final draft. All authors read and approved the final manuscript.

Details of Ethics Approval

The study received ethics approval from the Higher Degrees, Research and Ethics Committee at Makerere University on 15 February 2011 with the reference IRB00011353, Protocol (121).

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References

1. Victora CG, Requejo JH, Barros AJD, Berman P, Bhutta Z, Boerma T, et al. Countdown to 2015: a decade of tracking progress for maternal, newborn, and child survival. Lancet. 2015 Oct;
2. Levels & trends in child mortality 2015. New York: UNICEF, World Health Organization, World Bank Group, United Nations; 2015.
3. Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When? Why? How to make the data count? Lancet. 2011 Apr;377(9775):1448–63.
4. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? Lancet. 2005 Mar 11;365(9462):891–900.
5. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health [Internet]. 2016 Jan [cited 2016 Jan 20]; Available from: http://linkinghub.elsevier.com/retrieve/pii/S2214109X15002752

6. Lawn JE, Kinney MV, Black RE, Pitt C, Cousens S, Kerber K, et al. Newborn survival: a multi-country analysis of a decade of change. Health Policy Plan. 2012;27(suppl 3):iii6–28.
7. Asiki G, Baisley K, Newton R, Marions L, Seeley J, Kamali A, et al. Adverse pregnancy outcomes in rural Uganda (1996–2013): trends and associated factors from serial cross sectional surveys. BMC Pregnancy Childbirth. 2015 Oct 29;15(1):279.
8. McClure EM, Saleem S, Pasha O, Goldenberg RL. Stillbirth in developing countries: a review of causes, risk factors and prevention strategies. J Matern Fetal Neonatal Med. 2009 Jan 1;22(3):183–90.
9. Allanson ER, Muller M, Pattinson RC. Causes of perinatal mortality and associated maternal complications in a South African province: challenges in predicting poor outcomes. BMC Pregnancy Childbirth. 2015 Feb 15;15(1):37.
10. Aminu M, Unkels R, Mdegela M, Utz B, Adaji S, van den Broek N. Causes of and factors associated with stillbirth in low- and middle-income countries: a systematic literature review. BJOG Int J Obstet Gynaecol. 2014 Sep 1;121:141–53.
11. McClure EM, Pasha O, Goudar SS, Chomba E, Garces A, Tshefu A, et al. Epidemiology of stillbirth in low-middle income countries: A Global Network Study. Acta Obstet Gynecol Scand. 2011;90(12):1379–85.
12. Mondal D, Galloway TS, Bailey TC, Mathews F. Elevated risk of stillbirth in males: systematic review and meta-analysis of more than 30 million births. BMC Med. 2014 Nov 27;12(1):220.
13. Andargie G, Berhane Y, Worku A, Kebede Y. Predictors of perinatal mortality in rural population of Northwest Ethiopia: a prospective longitudinal study. BMC Public Health. 2013;13(1):168.
14. Debelew GT, Afework MF, Yalew AW. Determinants and Causes of Neonatal Mortality in Jimma Zone, Southwest Ethiopia: A Multilevel Analysis of Prospective Follow Up Study. PLoS ONE. 2014 Sep 18;9(9):e107184.
15. Gizaw M, Molla M, Mekonnen W. Trends and risk factors for neonatal mortality in Butajira District, South Central Ethiopia, (1987-2008): a prospective cohort study. BMC Pregnancy Childbirth. 2014 Feb 11;14(1):64.
16. Yaya Y, Eide KT, Norheim OF, Lindtjørn B. Maternal and Neonatal Mortality in South-West Ethiopia: Estimates and Socio-Economic Inequality. PLoS ONE. 2014 Apr 30;9(4):e96294.
17. Bekana Kebede, Abebaw Gebeyehu, Sharma HR, Sisay Yifru. Prevalence and associated factors of neonatal mortality in North Gondar Zone, Northwest Ethiopia. Ethiop J Health Dev. 2012;26(2):66–71.
18. Mekonnen Y, Tensou B, Telake DS, Degefie T, Bekele A. Neonatal mortality in Ethiopia: trends and determinants. BMC Public Health. 2013;13(1):483.
19. Engmann C, Walega P, Aborigo RA, Adongo P, Moyer CA, Lavasani L, et al. Stillbirths and early neonatal mortality in rural Northern Ghana. Trop Med Int Health. 2012 Mar 1;17(3):272–82.
20. Ha YP, Hurt LS, Tawiah-Agyemang C, Kirkwood BR, Edmond KM. Effect of Socioeconomic Deprivation and Health Service Utilisation on Antepartum and Intrapartum Stillbirth: Population Cohort Study from Rural Ghana. PLoS ONE. 2012 Jul 13;7(7):e39050.
21. Kayode GA, Ansah E, Agyepong IA, Amoakoh-Coleman M, Grobbee DE, Klipstein-Grobusch K. Individual and community determinants of neonatal mortality in Ghana: a multilevel analysis. BMC Pregnancy Childbirth. 2014 May 12;14(1):165.
22. Baiden F, Hodgson A, Adjuik M, Adongo P, Ayaga B, Binka F. Trend and causes of neonatal mortality in the Kassena–Nankana district of northern Ghana, 1995–2002. Trop Med Int Health. 2006 Apr 1;11(4):532–9.

23. Montagu D, Yamey G, Visconti A, Harding A, Yoong J. Where Do Poor Women in Developing Countries Give Birth? A Multi-Country Analysis of Demographic and Health Survey Data. PLoS ONE. 2011 Feb 28;6(2):e17155.
24. Nankabirwa V, Tumwine JK, Tylleskär T, Nankunda J, Sommerfelt H, Consortium PER, et al. Perinatal mortality in eastern Uganda: a community based prospective cohort study. PLoS One. 2011;6(5):e19674.
25. WHO, UNICEF. Every newborn: an action plan to end preventable deaths. Geneva: World Health Organization; 2014.
26. Lawn JE, Blencowe H, Oza S, You D, Lee AC, Waiswa P, et al. Every Newborn: progress, priorities, and potential beyond survival. Lancet. 2014 Jul 18;384(9938):189–205.
27. Waiswa P, Pariyo G, Kallander K, Akuze J, Namazzi G, Ekirapa-Kiracho E, et al. Effect of the Uganda Newborn Study on care-seeking and care practices: a cluster-randomised controlled trial. Glob Health Action. 2015 Mar 31;8:5–15.
28. World Health Organization. International statistical classification of diseases and related health problems. Vol. 1. Geneva: World Health Organization; 2004.
29. Waiswa P, Peterson S, Tomson G, Pariyo GW. Poor newborn care practices-a population based survey in eastern Uganda. BMC Pregnancy Childbirth. 2010;10(1):9.
30. Filmer D, Pritchett LH. Estimating wealth effects without expenditure data—or tears: An application to educational enrollments in states of india*. Demography. 2001;38(1):115–32.
31. Mosley WH, Chen LC. An Analytical Framework for the Study of Child Survival in Developing Countries. Popul Dev Rev. 1984 Jan 1;10:25–45.
32. Ibrahim S a., Babiker AG, Amin I k., Omer M i. a., Rushwan H. Factors associated with high risk of perinatal and neonatal mortality: an interim report on a prospective community-based study in rural Sudan. Paediatr Perinat Epidemiol. 1994 Apr 1;8(2):193–204.
33. Marete I, Tenge C, Pasha O, Goudar S, Chomba E, Patel A, et al. Perinatal Outcomes of Multiple-Gestation Pregnancies in Kenya, Zambia, Pakistan, India, Guatemala, and Argentina: A Global Network Study. Am J Perinatol. 2013 Mar 19;31(02):125–32.
34. de Lima Trindade L, Amestoy SC, Picolo D, Falchetti G, Milbrath VM. Fatores de risco para morte fetal no município de Pato Branco (Brasil). Risk factors for fetal death in the city of Pato Branco (Brazil). Investig Educ En Enferm. 2011;29(3):451–8.
35. Ezeh OK, Agho KE, Dibley MJ, Hall J, Page AN. Determinants of neonatal mortality in Nigeria: evidence from the 2008 demographic and health survey. BMC Public Health. 2014;14(1):521.
36. Selemani M, Mwanyangala MA, Mrema S, Shamte A, Kajungu D, Mkopi A, et al. The effect of mother's age and other related factors on neonatal survival associated with first and second birth in rural, Tanzania: evidence from Ifakara health and demographic surveillance system in rural Tanzania. BMC Pregnancy Childbirth. 2014;14(1):240.
37. Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the demographic and health surveys. Int J Gynecol Obstet. 2005;89:S7–24.
38. de Jonge H, Azad K, Seward N, Kuddus A, Shaha S, Beard J, et al. Determinants and consequences of short birth interval in rural Bangladesh: a cross-sectional study. BMC Pregnancy Childbirth. 2014;14(1):1–7.
39. Williams EK, Hossain MB, Sharma RK, Kumar V, Pandey CM, Baqui AH. Birth Interval and Risk of Stillbirth or Neonatal Death: Findings from Rural North India. J Trop Pediatr. 2008 Oct 1;54(5):321–7.
40. DaVanzo J, Hale L, Razzaque A, Rahman M. The effects of pregnancy spacing on infant and child mortality in Matlab, Bangladesh: how they vary by the type of pregnancy outcome that began the interval. Popul Stud. 2008;62(2):131–54.

41. Pebley AR, Stupp PW. Reproductive patterns and child mortality in Guatemala. Demography. 1987;24(1):43–60.
42. Aquino MMA de, Cecatti JG, Mariani Neto C. Risk factors associated to fetal death. Sao Paulo Med J. 1998 Nov;116(6):1852–7.
43. Mostafa G, Wojtyniak B, Fauveau V, Bhuiyan A. The relationship between sociodemographic variables and pregnancy loss in a rural area of Bangladesh. J Biosoc Sci. 1991;23(01):55–63.
44. Stringer EM, Vwalika B, Killam WP, Giganti MJ, Mbewe R, Chi BH, et al. Determinants of stillbirth in Zambia. Obstet Gynecol. 2011;117(5):1151–9.
45. Yatich NJ, Funkhouser E, Ehiri JE, Agbenyega T, Stiles JK, Rayner JC, et al. Malaria, intestinal helminths and other risk factors for stillbirth in Ghana. Infect Dis Obstet Gynecol. 2010;2010.
46. Kc A, Nelin V, Wrammert J, Ewald U, Vitrakoti R, Baral GN, et al. Risk factors for antepartum stillbirth: a case-control study in Nepal. BMC Pregnancy Childbirth. 2015 Jul 5;15(1):146.
47. Lamont K, Scott NW, Jones GT, Bhattacharya S. Risk of recurrent stillbirth: systematic review and meta-analysis. The BMJ. 2015 Jun 24;350:h3080.
48. Mokhtar MM, Abdel-Fattah MM. Consanguinity and advanced maternal age as risk factors for reproductive losses in Alexandria, Egypt. Eur J Epidemiol. 2001 Jun;17(6):559–65.
49. Lee AC, Mullany LC, Tielsch JM, Katz J, Khatry SK, LeClerq SC, et al. Community-based stillbirth rates and risk factors in rural Sarlahi, Nepal. Int J Gynecol Obstet. 2011 Jun;113(3):199–204.
50. Smith R, Maiti K, Aitken RJ. Unexplained antepartum stillbirth: A consequence of placental aging? Placenta. 2013 Apr 1;34(4):310–3.
51. Bashir AO, Ibrahim GH, Bashier IA, Adam I. Neonatal mortality in Sudan: analysis of the Sudan household survey, 2010. BMC Public Health. 2013;13(1):287.
52. Cleary-Goldman J, Malone FD, Vidaver J, Ball RH, Nyberg DA, Comstock CH, et al. Impact of maternal age on obstetric outcome. Obstet Gynecol. 2005;105(5, Part 1):983–90.
53. Mavalankar DV, Trivedi CR, Gray RH. Levels and risk factors for perinatal mortality in Ahmedabad, India. Bull World Health Organ. 1991;69(4):435–42.
54. Ali AAA, Elgessim ME, Taha E, Adam GK. Factors Associated with Perinatal Mortality in Kassala, Eastern Sudan: A Community-Based Study 2010–2011. J Trop Pediatr. 2014 Feb 1;60(1):79–82.
55. Akinyemi JO, Bamgboye EA, Ayeni O. Trends in neonatal mortality in Nigeria and effects of bio-demographic and maternal characteristics. BMC Pediatr. 2015 Apr 9;15(1):36.
56. Ronsmans C, Chowdhury ME, Alam N, Koblinsky M, Arifeen SE. Trends in stillbirths, early and late neonatal mortality in rural Bangladesh: the role of public health interventions. Paediatr Perinat Epidemiol. 2008 May 1;22(3):269–79.
57. Titaley C, Dibley M, Agho K, Roberts C, Hall J. Determinants of neonatal mortality in Indonesia. BMC Public Health. 2008;8(1):232.
58. Arokiasamy P, Gautam A. Neonatal mortality in the empowered action group states of India: trends and determinants. J Biosoc Sci. 2008;40(02):183–201.
59. Singh A, Kumar A, Kumar A. Determinants of neonatal mortality in rural India, 2007–2008. PeerJ. 2013;1:e75.
60. Ajaari J, Masanja H, Weiner R, Abokyi SA, Owusu-Agyei S. Impact of place of delivery on neonatal mortality in rural Tanzania. Int J MCH AIDS. 2012;1(1):49–59.
61. Cousens S, Blencowe H, Stanton C, Chou D, Ahmed S, Steinhardt L, et al. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. Lancet. 2011;377(9774):1319–30.
62. Haws RA, Mashasi I, Mrisho M, Schellenberg JA, Darmstadt GL, Winch PJ. “These are not good things for other people to know”: How rural Tanzanian women’s

experiences of pregnancy loss and early neonatal death may impact survey data quality. Soc Sci Med. 2010;71(10):1764–72.
63. Abou-Zahr CL, WHO, UNICEF, editors. Antenatal care in developing countries: promises, achievements and missed opportunities ; an analysis of trends, levels and differentials, 1990-2001. Geneva: World Health Organization; 2003. 32 p.
64. Robson M, Hartigan L, Murphy M. Methods of achieving and maintaining an appropriate caesarean section rate. Best Pract Res Clin Obstet Gynaecol. 2013 Apr 1;27(2):297–308.
65. Vogel JP, Betrán AP, Vindevoghel N, Souza JP, Torloni MR, Zhang J, et al. Use of the Robson classification to assess caesarean section trends in 21 countries: a secondary analysis of two WHO multicountry surveys. Lancet Glob Health. 2015 May;3(5):e260–70.