

Short Birth Intervals, Maternal Care, and Neonatal Mortality in Rwanda: A Facility-Based Retrospective Cohort Study Using Hierarchical Modelling

Nadine Niyomahoro¹, Mojeed Akorede Gbadamosi² 

¹Department of Public Health, School of Health Sciences, Mount Kenya University, Kigali, Rwanda; ²Department of Primary Healthcare, School of Medicine & Pharmacy, College of Medicine & Health Sciences, University of Rwanda, Kigali, Rwanda

Correspondence: Mojeed Akorede Gbadamosi, Department of Primary Healthcare, School of Medicine & Pharmacy, College of Medicine & Health Sciences, University of Rwanda, Kigali, Rwanda, Email gbojeed@yahoo.com

Background: Neonatal mortality remains a major public health concern in sub-Saharan Africa. Evidence from facility-based studies may be affected by selection and referral biases. This study examined the association between short birth intervals, maternal care, and other maternal, reproductive, and healthcare factors at different causal levels and neonatal mortality in a referral hospital in Rwanda, using a hierarchical modelling approach.

Methods: A retrospective cohort study was conducted among 1042 mother–neonate pairs admitted between 2022 and 2023. Variables were grouped into distal (socioeconomic), intermediate (reproductive), and proximal (clinical) levels. Sequential logistic regression models were applied. Due to substantial non-random missingness in birth interval data, complete-case analysis was used for intermediate model, with sensitivity analyses to assess robustness. A Directed Acyclic Graph was used to evaluate potential biases.

Results: Among 1,042 neonates, 32 (3.07%) died. Lower maternal education was associated with higher odds of neonatal mortality (aOR 2.18; 95% CI 1.08–4.54), although this may reflect selection bias. Short birth interval showed an inverse association with neonatal mortality, but this finding was unstable and not interpretable due to non-random missing data and bias. Proximal factors showed consistent associations: inadequate antenatal care (<4 visits) was associated with higher odds (aOR 3.12; 95% CI 1.29–7.54), and preterm birth was strongly associated (aOR 11.67; 95% CI 3.74–36.35).

Conclusion: Proximal clinical factors, particularly preterm birth and inadequate antenatal care, were consistently associated with neonatal mortality. Associations with distal and intermediate factors were affected by bias and missing data, limiting their interpretability. These findings underscore the need for caution when interpreting hospital-based data and highlight the value of hierarchical modelling with causal frameworks.

Plain Language Summary: Deaths during the first month of life remain a major problem in sub-Saharan Africa, including Rwanda. Although many women attend antenatal care, some newborns still die. Understanding why this happens can help improve care.

This study used hospital records from a referral hospital in Kigali to examine factors linked to newborn deaths. Instead of analysing all factors at once, we grouped them into three levels. First, we looked at social and reproductive factors such as education and number of previous pregnancies. Second, we examined birth spacing. Third, we assessed medical and healthcare-related factors, including antenatal care attendance and whether the baby was born too early.

We found that medical factors were most strongly linked to newborn deaths. Babies born too early and those whose mothers attended fewer antenatal care visits had a much higher risk of dying. Some other findings were unexpected. For example, shorter birth intervals appeared to be linked to lower risk. However, this is likely due to the type of data used. Because this study was based on hospital admissions, it may not include babies who died before reaching care. This can make some factors appear protective when they are not.

These results show that improving the quality of antenatal care and the management of preterm births is important for reducing newborn deaths. They also highlight that hospital-based data should be interpreted carefully, as they may not reflect what is happening in the wider population.

Keywords: antenatal care, birth spacing, hierarchical modeling, neonatal mortality, parity, Rwanda

Introduction

Neonatal mortality, defined as death within the first 28 days of life, remains a major contributor to global under-five mortality. An estimated 2.3 million neonatal deaths occurred worldwide in 2022, accounting for nearly half of all deaths among children younger than five years.¹ The burden is disproportionately concentrated in sub-Saharan Africa (SSA), where declines in child and post-neonatal mortality have outpaced those in neonatal mortality.² Understanding the factors associated with death during this period remains a public health priority, as achieving Sustainable Development Goal target 3.2 - reducing neonatal mortality to at least 12 per 1,000 live births by 2030 - depends on improving neonatal survival.³

Rwanda's near-universal health insurance coverage, high uptake of prenatal care services, and strengthened health system have all contributed to significant improvements in maternal and child health.^{4,5} Neonatal mortality still accounts for a significant portion of deaths in children under five, despite these advancements.^{5,6} This persistence implies that improvements in service quality, continuity of care, and management of high-risk pregnancies and newborns must accompany increases in service coverage. Evidence from referral hospitals, which handle the most complex and severe cases, can offer important insights into the factors that are associated with neonatal mortality in high-risk groups.⁷ However, because referral patterns, unequal access to care, and illness severity may skew observed relationships between social determinants and neonatal outcomes, analyses carried out in facility-based settings should be interpreted with caution.^{8–10}

It is critical to distinguish between facility-based and population-based research on newborn death. Population-based surveys (such as the Demographic and Health Surveys), which are generalisable but often lack clinical information, are used to record deaths at the community level. Even when facility-based studies like this one have comprehensive clinical data, they are vulnerable to confounding factors, including survival bias, admission criteria, and referral patterns, that can distort the relationships between social determinants and outcomes. This distinction is important when analysing outcomes from referral hospital settings.

Factors associated with neonatal mortality operate through interrelated pathways. The Mosley–Chen framework conceptualises child survival as the result of socioeconomic and demographic factors acting through intermediate behavioural and healthcare-related factors that are associated with proximate biological factors.¹¹

Building on this framework, it has been suggested to use hierarchical analytical techniques to prevent overadjustment when proximal and distal factors are included simultaneously, and to match statistical modelling with plausible causal ordering.¹² Ignoring this structure can obscure interpretation by conditioning on mediators or colliders, thereby biasing association estimates.^{11,13} Sequential modelling allows examination of how associations change as variables at different causal levels are introduced, providing insight into potential pathways without implying causality.

Most epidemiological studies of neonatal mortality in SSA rely on single-step multivariable models that provide fully adjusted estimates that combine distal and proximal factors.^{6,13} This approach may mask layered relationships between social, reproductive, and biological factors, particularly in facility-based datasets. Few studies have explicitly applied hierarchical modelling to neonatal mortality within referral hospital settings in SSA. Therefore, the primary objective of this study was to examine the association between short birth intervals, maternal care, and other maternal, reproductive, and healthcare factors at different causal levels, and neonatal mortality, in a referral hospital in Rwanda, using a hierarchical framework. A secondary objective was to assess how associations between distal factors and neonatal mortality change after sequential adjustment for intermediate and proximal factors.

Subject and Methods

Study Design and Setting

We conducted a retrospective cohort study among neonates admitted to the neonatology unit of Kibagabaga Level Two Teaching Hospital in Kigali, Rwanda, between January 1, 2022, and January 31, 2023. Kibagabaga Hospital is

a government-run district teaching hospital serving the Gasabo District primarily, and it receives referrals from neighbouring districts, including Kicukiro and Nyarugenge. The neonatology unit admits both inborn and referred neonates and manages a high volume of complicated neonatal cases.

Participants

The study population consisted of neonates aged 28 days or younger at the time of admission during the study period.

Inclusion Criteria Were

1. Age ≤ 28 days at admission;
2. Availability of neonatal outcome data (survival status)
3. Availability of maternal and obstetric information from medical records.

Neonates from multiple births (twins or higher-order multiples) were excluded because of their distinct risk profiles and because inclusion would complicate interpretation of birth interval effects. We acknowledge that this exclusion limits generalizability to high-risk neonatal populations in referral settings.

Records with missing outcome data were excluded.

A total of 1,042 mother–neonate pairs met the inclusion criteria and were included in the final analysis.

Data Collection

Data were extracted from archived paper records and the Open Clinic System electronic medical record using a structured data extraction tool developed for this study. The tool was informed by prior literature and clinical guidelines and pilot-tested on 10 records to ensure clarity and consistency.

Data extraction was performed independently by the lead investigator and two trained research assistants. Discrepancies were resolved through consensus.

Extracted variables included:

- Maternal sociodemographic characteristics
- Reproductive history
- Antenatal care utilisation
- Pregnancy complications
- Neonatal characteristics and outcomes.

Outcome Variable

The primary outcome was neonatal mortality, defined as death occurring within the first 28 days of life.

Exposure and Covariates

The primary exposure of interest was short birth interval, defined as the time (in months) between the index neonate and preceding live birth, categorized as:

Short: <24 months

Not short: ≥ 24 months

Covariates were grouped according to a hierarchical conceptual framework (Table 1):

Distal Factors (Socioeconomic and Reproductive)

- Maternal education (recoded as primary or less vs. secondary or higher)
- Parity (recoded as 0–2 vs. ≥ 3 previous pregnancies).

Table 1 Covariates by Causal Level and Operational Definitions

Causal Level	Covariate	Operational Definition	Type
Distal (socioeconomic/ reproductive)	Maternal education	Highest level completed: No formal education, Primary, Secondary, Tertiary	Categorical
	Parity	Total number of previous live births before the index neonate	Continuous
Intermediate	Birth interval	Time (in months) between index neonate and previous live birth; <24 months = short, ≥24 months = normal/long	Categorical (Short/Normal)
Proximal (biological/ healthcare)	Antenatal care (ANC) visits	Number of ANC visits during index pregnancy; categorized as <4 vs ≥4 as context-specific (Rwanda policy)	Binary / Categorical
	Pregnancy complications	Presence of any documented maternal complication during pregnancy (e.g., hypertension, gestational diabetes, infection)	Binary
	Gestational age	Completed weeks of gestation at birth; measured via last menstrual period or early ultrasound	Continuous

Intermediate Factor

- Birth interval (short vs. not short)

Proximal Factors (Biological and Healthcare-Related)

- Antenatal care (ANC) utilisation (adequate ≥4 visits vs. inadequate <4 visits, based on the national guidelines during the study period).
- Pregnancy complications (any documented vs. none)
- Gestational age at birth (preterm <37 weeks vs. term ≥37 weeks)

For transparency, original variable categories are presented in descriptive tables (Tables 2–4), while recoded variable categories were used in the regression models (Table 5).

Conceptual Framework and Modelling Strategy

We used a hierarchical conceptual framework to guide variable selection and model construction, distinguishing among distal, intermediate, and proximal levels.

We specified regression models sequentially rather than cumulatively:

- Model 1 (Distal): maternal education and parity (n=1,042)
- Model 2 (Distal + Intermediate): Model 1 variables + birth interval (restricted to complete cases, n=688)
- Model 3 (Proximal): antenatal care, pregnancy complications, and preterm birth (n=902)

To avoid overadjustment for mediators, we estimated Model 3 separately, excluding distal and intermediate variables.

Accordingly, coefficients across models should be interpreted as associations within each causal level rather than as changes in effect size.

Missing Data and Sensitivity Analysis

Birth interval data were missing for 354 participants (34%). Missingness was assessed by comparing characteristics between individuals with complete and incomplete data.

Table 2 Sociodemographic Characteristics of Mothers (n = 1042)

Characteristic	Category	Frequency (n)	Percentage (%)	Missing (n)
Maternal age^a	<20	50	4.8	0
	20 - 34	760	72.9	
	≥35	232	22.3	
	Median (IQR)	29.0 (10.0)		
	Min - Max	17 - 48		
Marital status	Married	837	80.3	0
	Separated	24	2.3	
	Single	179	17.2	
	Widowed	2	0.2	
Education level	No formal education	252	24.2	0
	Primary	386	37.1	
	Secondary	390	37.4	
	Tertiary	14	1.3	
Occupation	Unemployed	151	14.5	0
	Student	100	9.6	
	Self-employed	221	21.2	
	Other employment	570	54.7	
Monthly income (FRW)	<50,000	62	6.0	0
	50,000–99,999	102	9.8	
	100 000–199 999	282	27.1	
	200 000–299 999	156	15.0	
	≥300 000	16	1.5	
	I do not know	424	40.6	
Ubudehe category^δ	I	125	12.0	0
	II	835	80.1	
	III	82	7.9	
	IV	0	0.0	
Residence	Urban	1010	96.9	0
	Rural	32	3.1	
Household size (number of household members)	Small (1–2)	330	31.7	0
	Medium (3–5)	618	59.3	
	Large (6–9)	94	9.0	
	Median (IQR) ^a	3 (3)		
	Min - Max	1 - 9		

Notes: ^aVariable not normally distributed; Shapiro–Wilk test $p < 0.001$, median is reported. ^δUbudehe is Rwanda's community based socioeconomic classification system. Category I represents the poorest and most vulnerable households; Category II includes poor but not extremely poor households; Category III comprises resource rich households able to contribute to community development. Higher category (IV) exist but were not represented in this study. They are the wealthiest households.

Abbreviations: FRW, Rwanda Franc; IQR, Inter-quartile range; Min, Max, Minimum, Maximum.

Table 3 Obstetric and Health-Related Characteristics (n = 1042)

Characteristic	Category	Frequency (n)	Percentage (%)	Missing (n)
Birth interval (n=688)	Not short (≥24 months)	209	30.4	354
	Short (<24 months)	479	69.6	
Number of ANC visits (n=1020)^δ	Inadequate (<4)	343	33.6	22
	Adequate (≥4)	677	66.4	
Parity (Number of previous pregnancies)	0 - 2	776	74.5	0
	≥3	266	25.5	
Pregnancy Complications	Yes	276	26.5	0
	No	766	73.5	

Notes: ^δRwanda's protocol during the study used the 4 visit benchmark.

Abbreviations: ANC, Antenatal care; Min, Max, Minimum, Maximum.

Table 4 Neonates Characteristics (n = 1042)

Characteristic	Category	Frequency (n)	Percentage (%)	Missing (n)
Gestational age^a (n=858)	Extremely pre-term (<28 weeks)	8	0.9	184
	Very pre-term (28–31)	15	1.7	
	Moderate to late pre-term (32–36)	63	7.3	
	Term (37–41)	742	86.6	
	Post-term (≥42)	30	3.5	
	Median (IQR)	39.0 (2.0)		
	Min, Max	23.0, 46.0		
Birth weight (gram)^b	Very Low (<1500)	22	2.1	0
	Low (1500–2499)	68	6.5	
	Normal (2500–3999)	912	87.5	
	Macrosomia (≥4000)	40	3.8	
	Median (IQR)	3100.0 (62.6)		
	Min - Max	800.0, 5100.0		
APGAR Score (1 minute) (n=1041)	(Severely depressed (0–3)	42	4.0	1
	Depressed (4–6)	36	3.5	
	Normal (7–10)	963	92.5	
APGAR Score (5 minute) (n=1041)	(Severely depressed (0–3)	36	3.5	1
	Depressed (4–6)	14	1.3	
	Normal (7–10)	991	95.2	

Notes: ^aBased on AAP and ACOP (2006) classification; ^bBased on the WHO (2015) classification.

Abbreviations: IQR, Inter-quartile range; Min, Max, Minimum, Maximum.

Table 5 Multivariable Logistic Regression Models for Factors Associated with Neonatal Mortality (Model-Specific Analytic Samples)

Factor	Category	Model 1 aOR (95% CI)	Model 2 aOR (95% CI)	Model 3 aOR (95% CI)†
Education level	Secondary or higher (ref)	1.0	1.0	
	Primary or less	2.22 (1.08–4.54)*	2.12 (1.03–4.37)*	–
Parity	0 - 2 (ref)	1.0	1.0	
	≥3	1.95 (0.94–4.08)	1.10 (0.52–2.33)	–
Birth interval	Not short (≥24 months) (ref)	–	1.0	–
	Short (<24 months)	–	0.42 (0.20–0.85)*	–
Number of ANC visits (n=1020)	Adequate (≥4) (ref)	–	–	1.0
	Inadequate (<4)	–	–	3.13 (1.37–7.13)**
Pregnancy Complications	No (ref)	–	–	1.0
	Yes	–	–	1.77 (0.73–4.77)
Preterm birth (weeks)	No (≥37) (ref)	–	–	
	Yes (<37)	–	–	15.57 (6.95–34.88)***

Notes: *Statistically significant at $p < 0.05$, ** Statistically significant at $p < 0.01$, *** Statistically significant at $p < 0.001$. Model 1 (n=1042) and Model 2 (n=688 complete cases for birth interval) used standard logistic regression. Model 3 (n=902) used penalized maximum likelihood (Firth) logistic regression to obtain bias reduced estimates given the small number of events (32). Model 2: Model 1 + birth interval (intermediate factor). Reference categories: Secondary or higher maternal education, 0–2 parity, non-short birth interval, adequate ANC visit, absence of pregnancy complications, term gestation.

Abbreviations: aOR, Adjusted odds ratio; 95% CI, 95% Confidence interval.

Missingness was found to be non-random, as individuals with missing birth interval data differed systematically from those with complete data and had no recorded neonatal deaths. Given this, multiple imputation was considered inappropriate.

Therefore:

1. Analyses involving birth interval (Model 2) were restricted to complete cases
2. Sensitivity analyses were conducted using best-case (all missing = not short) and worst-case (all missing = short) scenarios ([Supplementary Tables S1–S2](#))

Findings related to birth interval were interpreted as non-inferential due to strong selection bias.

Figure 1 illustrates the hierarchical causal framework guiding covariate selection and sequential modelling. Distal factors (socioeconomic and reproductive) may influence neonatal mortality directly or indirectly through the intermediate factor (birth interval) and proximal biological/healthcare factors. This framework informed the construction of Models 1–3.

Bias Considerations

We anticipated several sources of bias due to the facility-based design:

1. **Selection and referral bias:** Admission depends on care-seeking behaviour, access, and illness severity.
2. **Survival bias:** Neonates who died before reaching the hospital were not included.
3. **Collider bias:** Conditioning on hospital admission, which may be influenced by both exposures and outcomes.

These mechanisms are illustrated in the Directed Acyclic Graph ([Supplementary Figure A1](#)) and were explicitly considered in the interpretation of results.

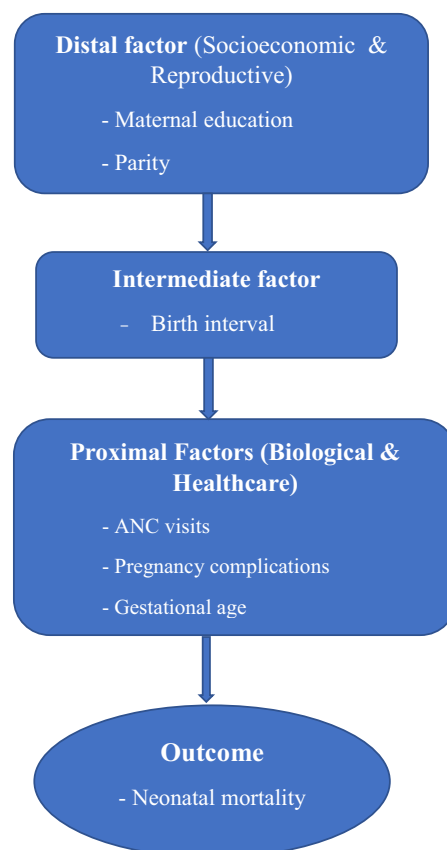


Figure 1 Hierarchical Framework for Neonatal Mortality.

Statistical Analysis

Descriptive statistics were used to summarise maternal, obstetric, and neonatal characteristics. Continuous variables were summarised using medians and interquartile ranges, and categorical variables using frequencies and percentages.

Logistic regression models were fitted sequentially according to the hierarchical framework. Model 1 (distal factors: maternal education and parity) included all 1,042 participants with complete data on these variables. Model 2 (distal + intermediate factor: birth interval) was restricted to the 688 participants with complete birth interval data, as missingness in this variable was substantial (34%). To assess the potential impact of missing birth interval data, sensitivity analyses were performed using best case (missing values assumed not short) and worst case (missing values assumed short) scenarios. Model 3 (proximal factors: antenatal care visits, pregnancy complications, and preterm birth) used penalized maximum likelihood (Firth) logistic regression to obtain bias reduced estimates, given the small number of events (32 deaths). This model was based on the 902 participants with complete data for all three predictors.

Hierarchical Modelling Approach

Models were estimated sequentially rather than cumulatively. Model 1 examined distal factors (maternal education and parity). Model 2 added the intermediate factor (birth interval) to Model 1. Model 3 examined proximal factors (antenatal care, pregnancy complications, preterm birth) separately, without including distal or intermediate variables. Therefore, Model 3 estimates should be interpreted as associations among proximal factors only, not as effects adjusted for distal determinants. This approach avoids overadjustment for mediators while allowing separate assessment of each hierarchical level.

Collinearity and Model Diagnostics

Variance inflation factors (VIFs) were examined for all models to ensure no collinearity issues; all VIFs were below 2.0. For standard logistic regression models (Models 1 and 2), goodness of fit was assessed using the Hosmer Lemeshow test, and the classification table was reviewed. For the Firth logistic regression model (Model 3), convergence was confirmed (five iterations) and profile likelihood confidence intervals were used, which are more reliable than Wald intervals in small samples.

Analyses were performed using IBM SPSS Statistics version 27 and Stata 15 (for Firth regression). Statistical significance was set at a two-sided p-value <0.05.

Results

A total of 1,042 mother–neonate pairs were included in the analysis, of which 32 (3.07%) resulted in neonatal death.

Descriptive Characteristics

Tables 2–4 present the maternal sociodemographic and reproductive characteristics, and neonatal characteristics. There were missing data for some variables, with birth interval (34.0%) and gestational age (17.7%) being the most important ones. Crucially, there were no recorded neonatal fatalities in instances where birth interval data were absent.

The median maternal age was 29 years (interquartile range [IQR], 10 years). Most mothers were aged 20–34 years, married, and residing in urban areas. Approximately one quarter had no formal education, and fewer than 2% had tertiary education (Table 2).

Birth interval data were available for 688 mothers (Table 3); among these, 69.6% had intervals shorter than 24 months. Adequate antenatal care attendance ($\geq$ four visits) was recorded for two-thirds of the participants. Pregnancy complications were documented in 26.5% of pregnancies. As shown in Table 4, the median gestational age at birth was 39 weeks (IQR 2), and 8.9% of neonates were born preterm. Low or very low birth weight was observed in 8.6% of neonates.

Table 5 presents the results of the sequential logistic regression models for distal, intermediate, and proximal variables in relation to neonatal mortality.

Distal Model

In the distal model, maternal education was associated with neonatal mortality. Mothers with primary education or less had higher odds of neonatal death compared to those with secondary education or higher (aOR 2.18; 95% CI 1.08–4.54; $p=0.030$). No significant association with parity was observed after adjustment.

Intermediate Model

The intermediate model included only complete cases ($n=688$) due to substantial missingness in the birth interval data. Short birth interval showed an inverse association with neonatal mortality (aOR 0.44; 95% CI 0.20–0.98; $p=0.045$), but this finding was unstable and not interpretable due to non-random missing data and bias. No neonatal deaths were observed among individuals with missing birth interval data. Sensitivity analyses showed variation in both the magnitude and direction of the association under different assumptions ([Supplementary Tables S1–S2](#)).

Proximal Model

In the proximal model, inadequate antenatal care attendance (<4 visits) was associated with neonatal mortality (aOR 3.12; 95% CI 1.29–7.54; $p=0.011$). Preterm birth was also associated with neonatal mortality (aOR 11.67; 95% CI 3.74–36.35; $p<0.001$). Pregnancy complications showed a non-significant positive trend.

Discussion

This facility-based retrospective cohort study applied a hierarchical modelling framework to examine how factors at different causal levels are associated with neonatal mortality in a referral hospital setting in Rwanda. The findings demonstrate that observed associations vary substantially across levels of analysis. Proximal clinical factors showed consistent, biologically plausible associations, whereas those involving distal and intermediate factors were highly sensitive to selection biases, referral patterns, and the inherent missing data in hospital-based datasets.^{11,12}

Distal and Intermediate Factors

Lower maternal education was associated with higher odds of neonatal mortality in the distal model. This direction is consistent with established evidence linking maternal education to improved health-seeking behaviour and child survival.^{14–16} However, in this setting, maternal education is also likely to be associated with the probability of hospital admission. More educated women may seek care earlier or be referred more frequently, while less educated women may present only when complications are severe or may not reach the facility at all.^{10,13}

As illustrated in the Directed Acyclic Graph ([Supplementary Figure A1](#)), conditioning on hospital admission, a variable that is associated with both exposure (education) and outcome (neonatal survival) can introduce collider bias.¹⁷ This mechanism can distort both the direction and magnitude of observed associations. Therefore, although the direction of association aligns with prior literature,^{14–16} the estimate should not be interpreted as a valid population-level association but rather as a context-specific association within a selected clinical population.

The inverse association observed between short birth interval and neonatal mortality requires particularly cautious interpretation. First, substantial non-random missingness was observed, with no neonatal deaths recorded among individuals with missing birth interval data. This indicates that the analytic sample for Model 2 represents a highly selected subgroup of the original cohort. Second, neonates born after short intervals who die before reaching the hospital are not captured in the dataset, introducing survival bias.¹⁸

These mechanisms are explicitly represented in the DAG ([Supplementary Figure A1](#)), where both birth interval and neonatal survival are associated with the probability of hospital admission. Conditioning on this variable induces collider bias, leading to spurious inverse associations.¹⁷ Sensitivity analyses further demonstrated instability in the magnitude and direction of this estimate under different assumptions about missing data.

Importantly, the observed inverse association contradicts well-established biological and epidemiological evidence linking short birth intervals to increased risk of adverse neonatal outcomes through mechanisms such as maternal

nutrition depletion¹⁹ and insufficient recovery time. Taken together, these findings indicate that the association between birth interval and neonatal mortality in the present study is not interpretable and should be considered non-inferential.

Parity showed a non-significant association in the distal model, which was attenuated after inclusion of birth interval. Previous studies suggest that the association of parity may operate through pathways such as birth spacing and maternal nutrition depletion.^{20,21} However, given the limitations described above, this pattern likely reflects overlapping pathways and selection effects rather than meaningful causal relationships.

Proximal Factors

In contrast, proximal clinical factors demonstrated consistent and plausible associations with neonatal mortality. Inadequate antenatal care attendance (<4 visits) was associated with a substantially higher odds of neonatal death. Antenatal care provides opportunities for early detection of complications, risk stratification, and timely referral, and inadequate attendance may reflect missed opportunities for intervention.²² We defined adequate antenatal care (≥ 4 visits) based on Rwanda's national protocol during the study period, while acknowledging that the current World Health Organisation recommendation is at least eight contacts.²³

Preterm birth showed the strongest association with neonatal mortality, consistent with studies identifying complications of prematurity as a leading cause of neonatal death.^{24–26} Unlike distal and intermediate factors, preterm birth is less associated with selection mechanisms related to care-seeking behaviour once admission has occurred, making it a more reliable indicator within facility-based datasets. The magnitude of the association observed in this study likely reflects the concentration of high-risk cases in referral hospital settings.

Pregnancy complications showed a positive but imprecise association, which may reflect limited statistical power, incomplete documentation, or selective referral of complicated cases to higher-level facilities.

Implications for Research and Practice

These findings have important implications. First, they highlight that facility-based datasets are well-suited for examining proximal clinical factors but are limited in their ability to estimate the associations of upstream factors, such as socioeconomic status and reproductive history.¹¹

Second, the results underscore the importance of explicitly accounting for selection and referral processes when analysing hospital-based data. Failure to do so may lead to misleading conclusions, particularly for variables such as birth interval and maternal education. The use of hierarchical modelling combined with causal diagrams, as applied in this study, provides a structured approach to identifying and interpreting these biases.

Third, future research examining distal and intermediate factors associated with neonatal mortality should prioritise population-based data or designs that better capture the full risk set, including births and deaths occurring outside health facilities.

From a practice perspective, the findings reinforce the importance of strengthening antenatal care utilisation and improving the management of preterm birth, which remain key targets for reducing neonatal mortality in referral settings.

Strengths and Limitations

This study has several strengths. It applies a clearly defined hierarchical conceptual framework, uses appropriate statistical methods including penalised regression for rare outcomes, and explicitly examines sources of bias, including selection and missing data. The integration of sensitivity analyses and a Directed Acyclic Graph strengthens the transparency and interpretability of the findings.

However, important limitations must be acknowledged. The facility-based design limits generalizability, as the study population represents a selected group of neonates who survived to admission and accessed care. Substantial non-random missingness in birth interval data restricts interpretation of intermediate-level analyses. The small number of events limits statistical precision. Exclusion of multiple births reduces generalizability to high-risk neonatal populations. Finally, some antenatal care quality variables were excluded from the regression models due to incomplete documentation.

Conclusion

In this referral hospital setting, proximal clinical factors, particularly preterm birth and inadequate antenatal care, showed consistent associations with neonatal mortality. In contrast, associations involving distal and intermediate factors were strongly affected by selection bias, referral patterns, and missing data and should not be interpreted as population-level associations. These findings highlight the limitations of facility-based datasets for examining upstream factors associated with and demonstrate the value of combining hierarchical modelling with causal frameworks to support appropriate interpretation.

Abbreviations

ANC, antenatal care; aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; IQR, interquartile range; LMIC, low- and middle-income countries; SDG, Sustainable Development Goal; SSA, Sub-Saharan Africa; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

Data Sharing Statement

The de-identified participant dataset and the analysis code used for this study are available from the corresponding author upon reasonable request and subject to review by the Mount Kenya University Ethics Committee and the participating hospital's administration to ensure participant confidentiality.

Ethics Approval and Informed Consent

This study was approved by the Mount Kenya University Ethics Committee (REF: MKU/ETHICS/23/01/2024(1)). Administrative permission to conduct the study was obtained from Kibagabaga Level Two Teaching Hospital. All participants provided written informed consent prior to participation. The study followed the principles of the Declaration of Helsinki.

Consent for Publication

Not applicable. No individual person's data in any form (including individual details, images, or videos) are included in the manuscript.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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