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Survival rates and associated factors for preterm neonates at Rev. John Chilembwe Hospital in Phalombe district in Malawi: a prospective cohort study

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Survival rates and associated factors for preterm neonates at Rev. John Chilembwe Hospital in Phalombe district in Malawi: a prospective cohort study

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Abstract

Background: Preterm neonatal mortality is high in resource-constrained settings such as district-based health facilities in Malawi. However, data on survival rates at each point in time and associated factors is scanty. We aimed to estimate survival rates and median overall survival (OS) time as well as assess time-to-death determinants of preterm neonates during the first 28 days of life at Rev. John Chilembwe Hospital in Phalombe district in Malawi.

Methods: Using a prospective cohort study design, we collected data on maternal age, gestational age, sex, HIV exposure, delivery mode, length of hospital stay, birthweight, Apgar score, birth place, respiratory distress, plurality, congenital anomaly, danger warning signs, vital signs and baby size of preterm neonates born and recruited from 01st January to 31st December, 2025. We followed-up each preterm neonate until death or censoring time. We estimated survival rates on day 1, 3, 7, 14, 21 and 28 using Kaplan-Meier curves. We planned to estimate median OS time but it was not reached during the 28-day follow-up period. We identified time-to-death determinants using Cox hazards proportion analysis.

Results: Of 136 preterm neonates followed-up, 55% (n = 75) were females. Median maternal age, gestational age, birthweight and initial body temperature were 23 years (interquartile range [IQR]: 20 years to 28 years), 33 weeks (IQR: 30 weeks to 34 weeks), 1,500g (IQR: 1,300g to 1,800g) and 35.10˚C (IQR: 34.50˚C to 35.95˚C), respectively. Survival estimates on day 1, 3, 7, 14, 21 and 28 were 91.2% (95% confidence interval [CI]: 86.5% to 96.1%), 80.9% (95% CI: 74.5% to 87.8%), 75.7% (95% CI: 68.9% to 83.3%), 72.8% (95% CI: 65.7% to 80.7%), 69.9% (95% CI: 62.6% to 78.0%) and 68.4% (95% CI: 61.0% to 76.7%), respectively. Each 100g increase in birthweight of preterm neonates reduced hazard of death by 19% (adjusted Hazard Ratio [aHR]: 0.81, 95% CI: 0.69 to 0.93, p<0.001).

Conclusion: Survival rates were low, with most deaths occurring in the first week of life. Lower birthweight was an important time-to-death determinant. Enhancing maternal nutrition, treatment of infections during pregnancy, early identification and management of preterm labor may help improve survival rates.

Keywords: Preterm, neonates, survival, mortality, factors, Malawi.

Introduction

Preterm birth refers to infants born alive before 37 completed weeks (less than 37 weeks) of gestation [1]. Prevalence of preterm births in 2020 was estimated at 9.9% worldwide [2]. Most of preterm births were in southern Asia (26.8% [36,099,000 of 134,767,000]) and sub-Saharan Africa (28.8% [38,819,300 of 134,767,000]) [2]. Global data, however, show that cases of preterm births had decreased by 5.26% between 1990 and 2019 (from 16.06 million to 15.22 million) [3]. In Malawi, the prevalence of preterm births was estimated at 14.5% (9.5% - 21.6%) in 2020 [2]. This is an increase from 10.5% (7.4 % - 14.3%) that was reported in 2014 [4]. Indeed, Malawi is among the leading countries with highest proportions of preterm births in the world. In 2020, only Bangladesh had the highest preterm prevalence in the world than Malawi estimated at 16.2% (11.8% - 21.7%) [2]. This results in adverse health outcomes for infants both in the short- and long-term. For example, prematurity is a risk factor for low birthweight [5]. Several studies highlight preterm birth complications as a leading cause of death among children under five years of age [1,6]. It is encouraging, however, to note that recent data have shown that preterm infant deaths had decreased by 47.71% between 1990 and 2019 (from 1.27 million to 0.66 million) [3].

Complications of preterm births continue to widen the gap of preterm deaths between high-income countries (HICs) and low and middle income countries (LMICs) [7]. For example, over 90% of extremely preterm (less than 28 weeks) born in developing countries die early whereas less than 10% of their counterparts die early in developed countries [1]. Several factors disadvantage the survival of preterm babies. Notably, low Apgar score at 5 min, hypothermia, jaundice, respiratory distress, maternal HIV status, preterm babies born before arrival, extremely preterm babies, very preterm babies and small for gestational age (SGA) have been highlighted to increase the risk of preterm neonatal mortality among others [8–13]. In low income African countries such as Malawi, however, preterm deaths are also compounded by various systemic factors that include high rates of teenage pregnancies, inadequate or lack of medical supplies and equipment as well as limited skills from midwives [14–16].

The recent routine reported data at the Rev. John Chilembwe Hospital estimated preterm neonatal mortality at 112 deaths per 1000 live preterm births (16 deaths per 143 preterm births) in 2023/24 Financial Year (FY). This is a high ratio that requires urgent and concerted efforts from all stakeholders at community, district and national levels. Notably, this ratio could even be higher if deaths of preterm neonates occurring after hospital discharge were to be included. It is, therefore, necessary to implement evidence-informed interventions in order to reverse this worrying trend. Specifically, to our knowledge, no published study has estimated the survival rates and assessed the time-to-death determinants of preterm neonates in Phalombe district. In general, few studies have followed up the preterm neonates in their respective homes and communities after the hospital discharge to estimate their survival rates and assess the time-to-death determinants in Malawi. Given this context, this study aimed to follow up both hospitalized and discharged preterm neonates born at and those referred to Rev. John Chilembwe Hospital to estimate their survival rates and median overall survival time as well as assess the time-to-death determinants in the first 28 days of life at this health facility in Phalombe district in southern Malawi.

Methods and materials

Study design and setting

We used a prospective cohort study design. This study was done at Rev. John Chilembwe Hospital in Phalombe district in southern Malawi. This is a secondary level and also the highest level of care at a district setting. The recruitment took place from 01st January to 31st December, 2025. Figure 1 shows the map of Phalombe district.

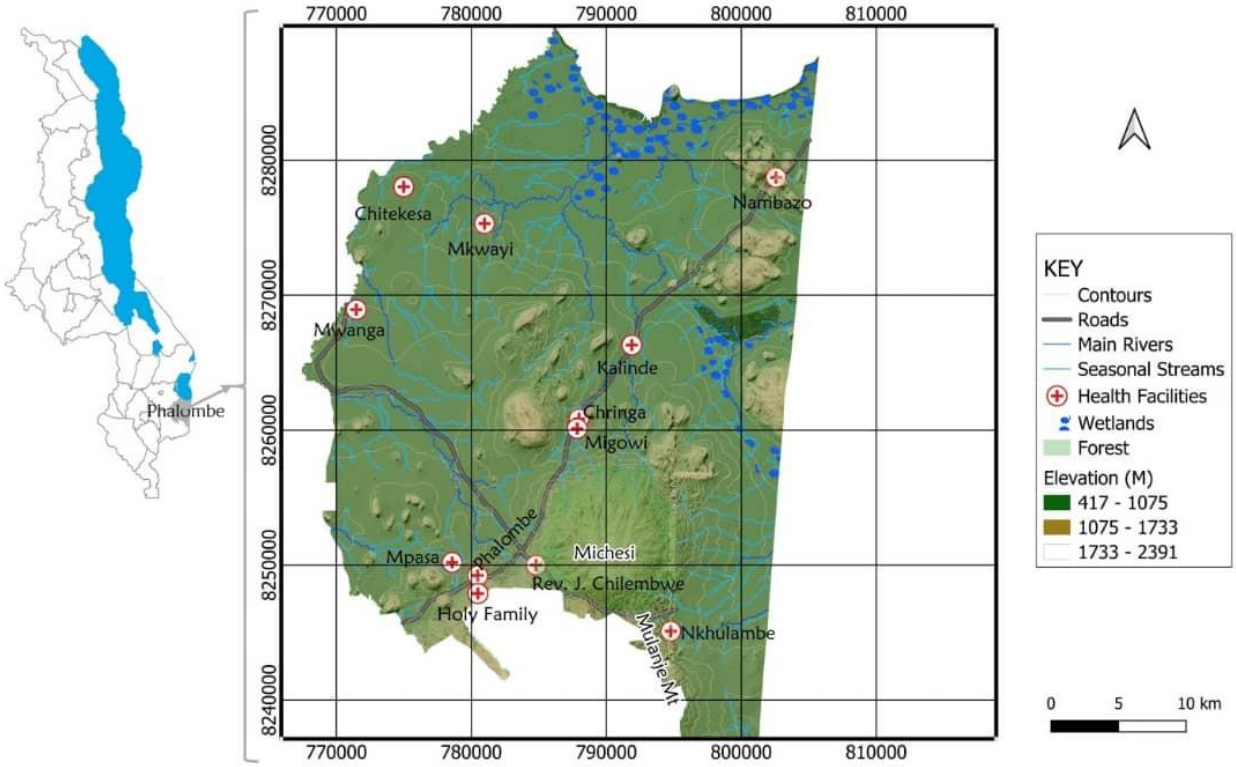


Figure 1: Map of Phalombe district

Study participants and Sample size

Our study participants were preterm neonates. Preterm neonates are babies born alive before 37 completed weeks of gestation. We recruited 136 preterm neonates born at Rev. John Chilembwe Hospital or referred from other health facilities throughout the study period between 01st January and 31st December, 2025. All preterm neonates born at or were referred to Rev. John Chilembwe Hospital within 24 hours of birth were included in the study. Preterm births that were referred to Rev. John Chilembwe Hospital after 24 hours had elapsed were excluded from the study as we could not observe other important parameters.

Data collection and follow-up

We developed a data collection tool which we used to collect sociodemographic and clinical data for the preterm neonates on their birthday. We followed up each preterm neonate in the first 28 days of their life to ascertain the outcome. The follow up was done either in hospital or in the community. We followed them up on day 1, 3, 7, 14, 21 and 28. Follow up in the hospital was done by the nurse/midwives who were part of the study team, whilst follow up in the community was done by health surveillance assistants (HSAs) who reported to the community-based maternal and child health coordinator on a daily basis.

Study variables and measurements

Table 1 shows both explanatory and outcome variables and how they were measured as continuous and categorical variables in this study.

Table 1: Study variables and measurements

Variable	Measurement
Explanatory variables	
Neonatal intrinsic factors	
Sex	
Female	Baby born female
Male	Baby born male
Gestational age was measured as both a continuous and a categorical variable (in weeks)	
Late preterm	34 weeks 0 days to 36 weeks 6 days
Moderately preterm	32 weeks 0 days to 33 weeks 6 days
Very preterm	28 weeks 0 days to 31 weeks 6 days
Extremely preterm	<28 weeks
Birthweight was measured as both a continuous and a categorical variable (in grams)	
Normal birthweight	≥2,500g
Low birthweight	1,500g to 2,499g
Very low birthweight	1,000g to 1,499g
Extremely low birthweight	<1,000g
Size of the baby*	
Appropriate for Gestational Age (AGA) at birth	10-90 percentiles
Small for Gestational Age (SGA) at birth	<10 percentiles
Large for Gestational Age (LGA) at birth	>90 percentiles
Clinical factors	
Respiratory distress	
No	SpO_2 >90% or Respiratory rate of <60 breaths per minute
Yes	SpO_2<90% or Respiratory rate of >60 breaths per minute
Unknown	Not recorded
Respiratory rate	
Normal	30-60 breaths per minute
Low	<30 breaths per minute
High	>60 breaths per minute
Unknown	Not recorded
Oxygen saturation (SpO_2)	
Normal	>90% on right atrial
Hypoxia	<90% on right atrial
Unknown	Not recorded
Apgar score at 5 mins	

	Normal	7-10
	Moderate birth asphyxia	4-6
	Severe birth asphyxia	0-3
Infection		
	Yes	Baby has any form of infection
	No	Baby does not have any form of infection
HIV exposure		
	Unexposed to HIV	Baby born to an HIV- mother
	Exposed to HIV	Baby born to an HIV+ mother
	Unknown	Baby born to a mother whose HIV status is unrecorded
Severe chest in-drawing		
	Yes	Baby has severe chest in-drawing
	No	Baby has no severe chest in-drawing
Fast breathing		
	Yes	>60 breaths per minute
	No	≤60 breaths per minute
Convulsions		
	Yes	Baby is convulsing
	No	Baby is not convulsing
No spontaneous movement		
	Yes	A complete lack of voluntary physical activity
	No	Self-generated motor activity or physical motion
Jaundice		
	Yes	Baby is diagnosed with jaundice
	No	Baby is not diagnosed with jaundice
Pulse rate		
	Normal	100-160 beats per minute
	Low	<100 beats per minute
	High	>160 beats per minute
Body temperature was measured as both a continuous and as a categorical variable (˚C)		
	Normothermia	36.5˚C - 37.5˚C
	Hypothermia	<36.5˚C
	Hyperthermia	>37.5˚C
	Unknown	Not recorded
Maternal and obstetric history		
Place of birth		
	This hospital	Rev. John Chilembwe Hospital
	In-transit	Born before arrival at Rev. John Chilembwe Hospital
	Other facility	Facilities other than Rev. John Chilembwe Hospital
	Home/Traditional Birth Attendant (TBA)	Non-institutional deliveries
Mode of delivery		
	Spontaneous vaginal delivery	Natural birth through vagina without the use of instruments
	Cesarean section	Surgical procedure to deliver a baby
	Assisted vaginal birth	Instrumental delivery
Maternal age (in years) was measured as a continuous variable and as a categorical variable		
	Adolescent girls	15-19 years
	Young women	20-24 years
	Mid-reproductive age women	25-34 years

	Women of advanced maternal age	≥35 years
	Unknown	Mother whose age is unrecorded or unknown
Outcome variable		
	Time-to-death (in days)	Time taken for preterm neonates from birth to death
	Alive or censored	Preterm neonates alive at the end of follow-up or end of study period

*We used Fenton Growth Calculator to measure size of the baby.

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Statistical analysis

Data were entered and cleaned in Microsoft Excel sheet then exported and coded for analysis in R. We performed descriptive analysis to calculate frequencies and percentages for categorical data. For continuous data, we calculated median values together with their corresponding interquartile ranges (IQR). This analysis included all 136 preterm neonates in the study dataset.

Survival probabilities were estimated using the Kaplan-Meier method and compared across categorical characteristics using log-rank tests. We estimated the survival probabilities on day 1, 3, 7, 14, 21 and 28. Univariable Cox proportional hazards models estimated crude hazard ratios (HRs) with 95% confidence intervals. The a priori adjusted model included sex, maternal age category, gestational age, and birthweight, with asphyxia, respiratory distress, infection, and congenital anomaly included as clinically important covariates. Because the number of deaths per model degree of freedom was low, adjusted point estimates were obtained from the Cox model and 95% confidence intervals were estimated using 500 nonparametric bootstrap samples with a fixed random seed of 123. Adjusted p-values are the two-sided Wald p-values from the fitted Cox model; confidence intervals and p-values were interpreted together, with statistical significance defined by a 95% confidence interval that did not cross HR = 1. A p-value of less than 0.05 was considered statistically significant.

Before analysis, missing categorical values were replaced with the most frequently observed category (mode), and missing continuous values were replaced with the sample median calculated from the observed values. Maternal age was imputed on the continuous years scale and then reclassified into the four legend-defined categories. Survival time and the death indicator were not imputed. A post-imputation completeness check verified that all variables used in the survival and adjusted Cox analyses contained zero missing values. There was no strong evidence that the proportional hazards assumption was violated for the final model (global p=0.557). The model concordance was 0.724, indicating reasonable discriminatory ability. We planned to estimate median OS time but it was not reached during the 28-day follow-up period.

Results

Baseline characteristics of preterm neonates by 28-day survival status at Rev. John Chilembwe Hospital, Phalombe District, Malawi

Table 2 shows baseline characteristics of preterm infants at Rev. John Chilembwe Hospital in southern Malawi. Among 136 preterm neonates followed up, 55% (n=75) were females. Overall median maternal age was 23 years (interquartile range [IQR]: 20 years to 28 years). Overall median birthweight was 1,500g (IQR: 1,300g to 1,800g). Overall median gestation week was 33 weeks (IQR: 30 weeks to 34 weeks). Overall median body temperature was 35.10˚C (IQR: 34.50˚C to 35.95˚C).

Table 2: Baseline characteristics of preterm neonates by 28-day survival status at Rev. John Chilembwe Hospital, Phalombe District, Malawi

Characteristic	Alive/Censored **N = 93**[1]	Died **N = 43**[1]	Overall **N = 136**[1]
Sex			
Female	51 (55%)	24 (56%)	75 (55%)
Male	42 (45%)	19 (44%)	61 (45%)
Maternal age (years), continuous	24 (19, 28)	23 (20, 28)	23 (20, 28)
Maternal age (years)			
15-19	25 (27%)	8 (19%)	33 (24%)
20-24	27 (29%)	18 (42%)	45 (33%)
25-34	33 (35%)	13 (30%)	46 (34%)
>=35	8 (8.6%)	4 (9.3%)	12 (8.8%)
Birthweight (g)	1,600 (1,400, 1,900)	1,300 (900, 1,600)	1,500 (1,300, 1,800)
Birthweight category			
Low birthweight	66 (71%)	16 (37%)	82 (60%)
Very low birthweight	25 (27%)	16 (37%)	41 (30%)
Extremely low birthweight	2 (2.2%)	11 (26%)	13 (9.6%)
Gestational age (weeks)	34.00 (31.30, 35.00)	32.00 (30.00, 34.00)	33.00 (30.00, 34.00)
Gestational age category			
Late preterm	49 (53%)	15 (35%)	64 (47%)
Moderately preterm	20 (22%)	11 (26%)	31 (23%)
Very preterm	23 (25%)	14 (33%)	37 (27%)
Extremely preterm	1 (1.1%)	3 (7.0%)	4 (2.9%)
Plurality			
Singleton birth	78 (84%)	31 (72%)	109 (80%)
Multiple births	15 (16%)	12 (28%)	27 (20%)
Place of birth			
This facility	55 (59%)	24 (56%)	79 (58%)
In-transit/BBA	9 (9.7%)	2 (4.7%)	11 (8.1%)
Other facility	24 (26%)	14 (33%)	38 (28%)
Home/TBA	5 (5.4%)	3 (7.0%)	8 (5.9%)
HIV exposure			
Unexposed to HIV	89 (96%)	41 (95%)	130 (96%)
Exposed to HIV	4 (4.3%)	2 (4.7%)	6 (4.4%)
Apgar score at 5 minutes			
4	2 (2.2%)	4 (9.3%)	6 (4.4%)
5	0 (0%)	1 (2.3%)	1 (0.7%)
6	2 (2.2%)	1 (2.3%)	3 (2.2%)
7	8 (8.6%)	2 (4.7%)	10 (7.4%)
8	18 (19%)	7 (16%)	25 (18%)

9	20 (22%)	12 (28%)	32 (24%)
10	43 (46%)	16 (37%)	59 (43%)
Asphyxia			
No Asphyxia	89 (96%)	37 (86%)	126 (93%)
Moderate Asphyxia	4 (4.3%)	6 (14%)	10 (7.4%)
Severe Asphyxia	0 (0%)	0 (0%)	0 (0%)
Mode of delivery			
Spontaneous Vaginal Delivery	76 (82%)	39 (91%)	115 (85%)
Caesarean Section	17 (18%)	4 (9.3%)	21 (15%)
Convulsions	2 (2.2%)	0 (0%)	2 (1.5%)
No spontaneous movements	6 (6.5%)	6 (14%)	12 (8.8%)
Severe chest in-drawing	19 (20%)	17 (40%)	36 (26%)
Fast breathing	7 (7.5%)	10 (23%)	17 (13%)
Infection	29 (31%)	15 (35%)	44 (32%)
Jaundice	3 (3.2%)	1 (2.3%)	4 (2.9%)
Congenital anomaly	7 (7.5%)	3 (7.0%)	10 (7.4%)
Body temperature (°C)	35.30 (34.80, 36.00)	34.90 (33.90, 35.60)	35.10 (34.50, 35.90)
Temperature category			
Normothermia	13 (14%)	6 (14%)	19 (14%)
Hypothermia	78 (84%)	36 (84%)	114 (84%)
Hyperthermia	2 (2.2%)	1 (2.3%)	3 (2.2%)
Respiratory rate (breaths/min)	48 (42, 53)	48 (40, 60)	48 (42, 55)
Oxygen saturation (%)	93 (85, 97)	91 (80, 96)	93 (83, 97)
Respiratory distress	35 (38%)	24 (56%)	59 (43%)
Pulse rate (beats/min)	143 (131, 152)	124 (101, 145)	139 (124, 149)
Pulse rate category			
Normal	80 (86%)	32 (74%)	112 (82%)
Low	1 (1.1%)	8 (19%)	9 (6.6%)
High	12 (13%)	3 (7.0%)	15 (11%)
Oxygen saturation category			
Normal	64 (69%)	24 (56%)	88 (65%)
Hypoxia	29 (31%)	19 (44%)	48 (35%)
Baby size			
Appropriate for Gestational Age	42 (45%)	11 (26%)	53 (39%)
Small for Gestational Age	49 (53%)	31 (72%)	80 (59%)
Large for Gestational Age	2 (2.2%)	1 (2.3%)	3 (2.2%)

[1]n (%); Median (Q1, Q3); Continuous variables are reported as median (Q1, Q3) and categorical variables as n (%). Maternal age is shown both continuously and in legend-defined categories. No missing values remained in analysis variables after pre-specified imputation.

Overall Kaplan-Meier Survival probabilities at Rev. John Chilembwe Hospital in Phalombe district, Malawi

Figure 2 shows the overall Kaplan-Meier Survival probabilities at Rev. John Chilembwe Hospital in Phalombe district, southern Malawi. Overall survival probabilities were 91.2% (95% confidence interval [CI]: 86.5% to 96.1%) on day 1, 80.9% (95% CI: 74.5% to 87.8%) on day 3, 75.7% (95% CI: 68.9% to 83.3%) on day 7, 72.8% (95% CI: 65.7% to 80.7%) on day 14, 69.9% (95% CI: 62.6% to 78.0%) on day 21 and 68.4% (95% CI: 61.0% to 76.7%) on day 28.

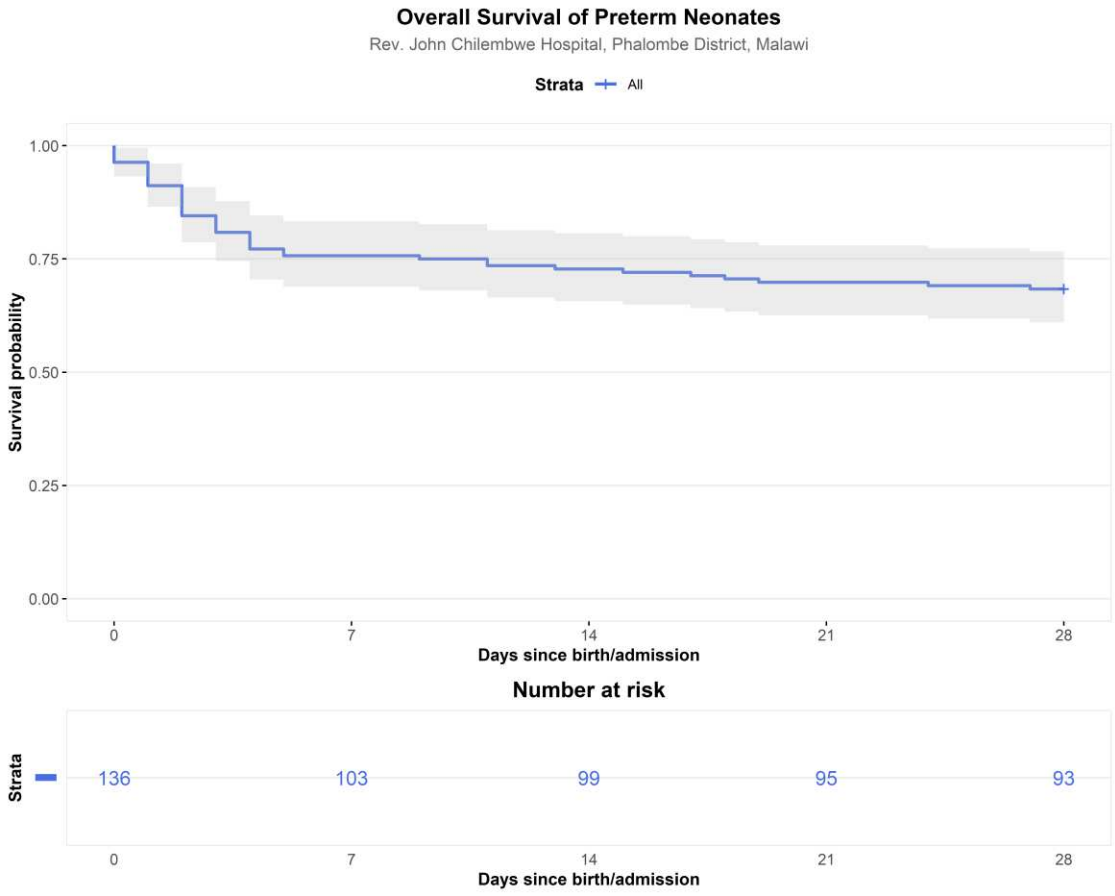


Figure 2: Overall survival probabilities of preterm neonates at Rev. John Chilembwe Hospital in Phalombe district in Malawi.

Crude and Adjusted Cox Proportional Hazards Regression for 28-day mortality among preterm neonates

Table 3 shows results for the Crude and Adjusted Cox Proportional Hazards Regression Analysis for 28-day mortality among preterm neonates at Rev. John Chilembwe Hospital in Malawi. In the Crude Cox Proportional Hazards Regression, we observed that one week increase in gestational age reduced the hazard of death by 15% (crude Hazard Ratio = 0.85, [95% CI: 0.76 to 0.95], p=0.004). Moderate asphyxia increased the hazard of death by 170% (crude Hazard Ratio = 2.70, [95% CI: 1.14 to 6.42], p=0.024). Severe chest in-

drawing increased the hazard of death by 117% (crude Hazard Ratio = 2.17, [95% CI: 1.18 to 4.00], p=0.013). Fast breathing increased the hazard of death by 185% (crude Hazard Ratio = 2.85, [95% CI: 1.40 to 5.81], p=0.004). Respiratory distress increased the hazard of death by 97% (crude Hazard Ratio = 1.97, [95% CI: 1.08 to 3.59], p=0.028). Low pulse rate increased the hazard of death by 641% (crude Hazard Ratio = 7.41, [95% CI: 3.37 to 16.30], p<0.001). Small for gestational age increased the hazard of death by 106% (crude Hazard Ratio = 2.06, [95% CI: 1.03 to 4.09], p=0.040).

In the Adjusted Cox Proportional Hazards Regression, we found that each 100g increase in birthweight was associated with a 19% reduction in hazard of death (adjusted Hazard Ratio [aHR]: 0.81, 95% CI: 0.69 to 0.93, p<0.001). The following variables were not associated with hazard of death; sex [male vs female] (aHR: 1.36, 95% CI: 0.64 to 3.44, p=0.357), maternal age: [20-24 years vs 15-19 years] (aHR: 1.08, 95% CI: 0.38 to 3.94, p=0.087), maternal age: [25-34 years vs 15-19 years] (aHR: 1.17, 95% CI: 0.37 to 3.92, p=0.734), maternal age: [≥35 years vs 15-19 years] (aHR: 2.15, 95% CI: 0.36 to 7.58, p=0.239), gestational age: [per 1 week increase] (aHR: 1.00, 95% CI: 0.85 to 1.16, p=0.958), asphyxia: [moderate asphyxia vs no asphyxia] (aHR: 2.19, 95% CI: 0.58 to 9.16, p=0.146), Respiratory distress: [Yes vs No] (aHR: 2.00, 95% CI: 0.98 to 4.90, p=0.120), Infection: Yes (vs No) (aHR: 0.74, 95% CI: 0.28 to 1.51, p=0.388), Congenital anomaly: [Yes vs No] (aHR: 1.79, 95% CI: 0.00 to 9.09, p=0.356).

Table 3: Crude and Adjusted Cox Proportional Hazards Regression for 28-day mortality among preterm neonates

	Category	Crude HR	CI	P-value	Adjusted HR	CI	P-value
Sex	sex_fMale	1.02	0.56 to 1.86	0.949	1.36	0.64 to 3.44	0.357
Maternal age (years)	maternal_age_group20-24	1.84	0.80 to 4.24	0.150	1.08	0.38 to 3.94	0.871
Maternal age (years)	maternal_age_group25-34	1.21	0.50 to 2.92	0.670	1.17	0.37 to 3.92	0.734
Maternal age (years)	maternal_age_group>=35	1.65	0.50 to 5.47	0.416	2.15	0.36 to 7.58	0.239
Gestational age (weeks)	gestation_weeks	0.85	0.76 to 0.95	**0.004**	1.00	0.85 to 1.16	0.958
Birthweight (g)	birthweight_g	1.00	1.00 to 1.00	**<0.001**	0.81	0.69 to 0.93	**<0.001**
Gestational age category	gestation_catModerately preterm	1.61	0.74 to 3.51	0.230			
Gestational age category	gestation_catVery preterm	1.84	0.89 to 3.80	0.102			
Gestational age category	gestation_catExtremely preterm	3.59	1.04 to 12.43	**0.044**			
Birthweight category	birthweight_catVery low birthweight	2.21	1.10 to 4.41	**0.025**			
Birthweight category	birthweight_catExtremely low birthweight	7.52	3.45 to 16.39	**<0.001**			
Plurality	plurality_fMultiple births	1.91	0.98 to 3.73	0.056			
Place of birth	place_of_birth_fIn-transit/BBA	0.56	0.13 to 2.38	0.434			
Place of birth	place_of_birth_fOther facility	1.40	0.72 to 2.70	0.319			
Place of birth	place_of_birth_fHome/TBA	1.42	0.43 to 4.73	0.564			
HIV exposure	hiv_exposure_fExposed to HIV	1.09	0.26 to 4.51	0.904			
Asphyxia	asphyxia_fModerate Asphyxia	2.70	1.14 to 6.42	**0.024**	2.19	0.58 to 9.16	0.146
Asphyxia	asphyxia_fSevere Asphyxia	NA	NA	NA			
Mode of delivery	mode_of_delivery_fCaesarean Section	0.49	0.17 to 1.36	0.170			
Convulsions	convulsions_fYes	0.00	0.00 to Inf	0.996			
No spontaneous movements	no_movement_fYes	1.99	0.84 to 4.72	0.118			
Severe chest in-drawing	chest_drawing_fYes	2.17	1.18 to 4.00	**0.013**			
Fast breathing	fast_breathing_fYes	2.85	1.40 to 5.81	**0.004**			
Infection	infection_fYes	1.14	0.61 to 2.13	0.687	0.74	0.28 to 1.51	0.388
Jaundice	jaundice_fYes	0.68	0.09 to 4.95	0.705			
Congenital anomaly	congenital_anomaly_fYes	0.92	0.28 to 2.96	0.882	1.79	0.00 to 9.09	0.356
Temperature category	temp_catHypothermia	1.02	0.43 to 2.43	0.958			
Temperature category	temp_catHyperthermia	1.24	0.15 to 10.31	0.841			
Respiratory distress	respiratory_distress_fYes	1.97	1.08 to 3.59	**0.028**	2.00	0.98 to 4.9	0.120
Pulse rate category	pulse_catLow	7.41	3.37 to 16.30	**<0.001**			
Pulse rate category	pulse_catHigh	0.63	0.19 to 2.05	0.441			
Baby size	baby_size_fSmall for Gestational Age	2.06	1.03 to 4.09	**0.040**			
Baby size	baby_size_fLarge for Gestational Age	1.50	0.19 to 11.61	0.699			

HR = Hazard Ratio; CI = Confidence Interval; Respiratory Distress is defined as either SpO_2 of <90% or respiratory rate of >60 breaths per minute, Maternal age is included as an a priori variable in the adjusted model; P-values in bold indicate statistical significance at <0.05

Discussion

We aimed to estimate survival rates and median OS time as well as assess determinants of time-to-death among preterm neonates at Rev. John Chilembwe Hospital in Phalombe district in southern Malawi during the first 28 days of life. The United Nations through its Sustainable Development Goal number 3 (SDG #3) on good health and well-being, specifically under sub SDG #3.2 aims to increase neonatal survival rate to at least 98.8% or more (12 or fewer neonatal deaths per 1000 live births) by 2030 [17]. Since 2015/2026 to 2024, trends in overall national neonatal survival rate have modestly increased from 97.3% to 97.6% (27 to 24 neonatal deaths per 1,000 live births as in 2024) in Malawi [18]. In Malawi, the target is to have an overall neonatal survival rate of 98.3% (17 neonatal deaths per 1,000 live births) by 2030 [14]. There is no target specifically for preterm neonatal mortality in the country. Our study, however, established a low survival rate for preterm neonates of 68.4%. This finding was identical to a 66.5% survival rate of preterm neonates observed in an Ethiopian study [19]. In our study, most deaths occurred in the first week of life with a survival rate of 75.7%. Our finding is consistent with findings from other two Ethiopian studies which observed that first week of preterm infants was the hazard time to death [20,21]. Over half (52.4%) of early neonatal deaths occurred in the first two days of life according to Ethiopian Public Health Institutes (EPHI) which collected, analyzed and compiled data from various health facilities across the country [20]. This is in agreement with findings from another Ethiopian study done in five public hospitals of Addis Ababa which reported that the first seven days of admission was the hazard time to death with median time of six days [21]. Comprehensive care for preterm neonates in the early days of their lives is paramount to improving their survival time.

We planned to estimate median OS time but it was not reached during the 28-day follow-up period. Some studies aimed to estimate median OS time among preterm neonates in Ethiopia and Zambia, however, had reported median OS times of 18 days and 4.08 days (IQR, 1.42 to 15) during the 28-day follow-up period, respectively [19,22]. All the preterm neonates were admitted to neonatal intensive care unit (NICU) in an Ethiopian study whereas 65.4% (2116/3236) of the preterm neonates were admitted to NICU in a Zambian study. Nonetheless, the cohort of preterm neonates at Rev. John Chilembwe Hospital had performed better during the 28-day follow-up period than their colleagues in an Ethiopian and Zambian studies. This may be due to differences in clinical, medical, maternal and obstetric history as well as neonatal intrinsic factors among other reasons.

We also observed that each 100g increase in birthweight of preterm neonates was associated with a 19% reduction in hazard of death (aHR: 0.81, 95% CI: 0.69 to 0.93, $p<0.001$). This is consistent with another Malawian study which established that an increase in birthweight resulted in higher survival rates of preterm neonates [23] as well as findings of other studies elsewhere [21,24]. For example, data from the United States of America indicated that an increase in infant birthweight resulted in lower mortality rates [24]. Similar findings were observed from an Ethiopian study that reported that the median hazard time to death of extremely low birthweight was 3 days whereas that of very low birthweight was 5 days and this was shorter than time-to-death of 7 days for neonates having normal birthweight [21]. Notably, birthweight has been highlighted as an important and strong indicator of maternal and newborn health as well as nutrition [25]. It is, therefore,

important to improve quality of antenatal care which will enhance maternal nutrition, treatment of infections during pregnancy, early identification and management of preterm labor as this may help improve survival rates in this setting [26].

Strengths and limitations of the study

The main strength of this study is that we used a prospective cohort study design which is appropriate to establish time-to-death temporal relationship. Prospective cohort studies, however, have some limitations. First, they are observational in nature as such they are unable to control for unknown confounders as is the case with randomized controlled trials. Second, we did not collect and adjust for all plausible sociodemographic and clinical data in our final model. Third, we recorded survival time as 0 days for babies who were born and died on the same day. Recording the exact time of birth and death could have allowed us to calculate the actual survival time in hours and convert to days i.e. 12 hours = 0.5 days. Fourth, the sample size limited the number of variables that could be included in the adjusted model while maintaining adequate events per variable. Fifth, although the analysis dataset was complete after pre-specified imputation, median and mode imputation can reduce variability and understate uncertainty. Finally, as a single-center study, the results may not be generalizable to other settings in Malawi.

Conclusion

Survival estimates for preterm neonates were low, with most deaths occurring in the first week of life. Specifically, 91.2%, 80.9%, 75.7%, 72.8%, 69.9% and 68.4% of preterm neonates survived beyond day 1, 3, 7, 14, 21 and 28, respectively. Lower birthweight was an important time-to-death determinant. Enhancing maternal nutrition, treatment of infections during pregnancy, early identification and management of preterm labor may help improve survival rates.

List of abbreviations

aHR: Adjusted Hazard Ratio

AGA: Appropriate for Gestational Age

BBA: Born Before Arrival

cHR: Crude Hazard Ratio

CI: Confidence Interval

EPHI: Ethiopian Public Health Institutes

HICs: High-Income Countries

HSAs: Health Surveillance Assistants

IQR: Interquartile Ranges

LBW: Low Birthweight

LGA: Large for Gestational Age

LMICs: Low and Medium Income Countries

OS: Overall Survival time

SGA: Small for Gestational Age

SpO_2: Oxygen Saturation

TBA: Traditional Birth Attendant

Declarations

Ethics approval and consent to participate

Kamuzu University of Health Sciences Research Ethics Committee [KUREC] (formerly College of Medicine Research Ethics Committee [COMREC] approved this study (approval number: P.10/24-1161). Informed consent to participate was obtained in writing from legal guardians of the neonates. All methods were performed according to the relevant guidelines and regulations as outlined in the Helsinki Declaration.

Consent for publication

Not applicable.

Data availability statement

All data generated or analyzed during this study are included in this published article.

Competing interests

All authors have no conflicts of interest to declare that are relevant to the content of this article.

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Authors' contributions

DM, TT, VM, GZ, EL and FMM conceptualized the study as well as enrolled study participants, conducted follow ups and collected data. DM and FMM supervised the study and drafted the first manuscript. WFN performed formal data analysis. TT, GZ, VM, GM, EL, WFN, SK, GP, PM, CP, MP, EC, EB, GC and SK reviewed and edited the first manuscript. All authors approved the final manuscript.

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