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Predictors of neonatal mortality in Tigray Regional State, Northern Ethiopia: a comparison of parametric survival models' approaches

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Abstract

Background: *The neonatal age is the most vulnerable time for survival in which children appeare at the highest risk of dying in their lives. Ethiopia has pledged to lower under-five child mortality rates since 2015 despite being one of the SSA nations to have achieved the fourth Millennium Development Goal (MDG4). The neonatal mortality rate (NMR) is still a significant public health issue in Ethiopia, and it is getting worse in the Tigray region. Neonatal mortality dataset from retrospective cross-sectional study research is also scarce. The objective of this study was to assess the predictors of neonatal mortality in the Tigray region of northern Ethiopia.*

Method: *A retrospective cross-sectional study design was conducted from 18, January, 2016 to 27, June 2016. In this study a total of 716 neonates were selected. Neonatal mortality risk factors include predictor variables such as neonate and mother demographics, health, and environmental factors. The study used descriptive statistics, Kaplan-Meier comparisons, and parametric survival models, and comparisons were also performed to select suitable forecasting model analyses.*

Result: *The overall NMR experienced was 4.3 neonatal deaths per 100 total live births. The estimated mean follow-up time of neonates was 10.0 days [95% CI: 9.67, 10.30] in the Tigray region. The multivariable Weibull-regression model analysis revealed that predictors being multiple birth type (AHR = 10.9, 95% CI: 3.4, 35.5) and home delivery (AHR = 10.5, 95% CI: 3.0, 36.6) were critically important risk predictors associated with a higher NMR.*

Conclusion: *The prevalence of NMR showed that the NMR in the Tigray region was greater than the national average.The current study identified the multiple birth type and home delivery of the neonates as crucial predictor factors for NMR. Interventions should be improved to these factors that significantly decrease the NMR problem among neonates.*

Introduction

Neonatal Mortality Rate (NMR) is the risk that a newborn will die within the first 28 days of life, or the first 4 weeks of life (1). It is given as the number of neonatal fatalities per 1,000 live births. The period of neonatal starts at birth and ends at 28 completed days after birth. It is the time when a neonate's survival status is most vulnerable (2).

According to (3), 2.9 million newborns globally perished within their first month of life each year, with the majority of these deaths taking place in underdeveloped nations. Preterm neonates have an extremely low survival rate in impoverished nations (3).

According to the 2022 Global Report, central and southern Asia had the second-highest NMR of 23 deaths per 1000 total live births, accounting for 36% of all newborn deaths worldwide, after Sub-Saharan Africa (SSA), with 27 deaths per 1000 live births and 43% of all newborn deaths worldwide. In addition, a child born in SSA has a ten-fold higher risk of dying than a child born in a high-income nation (4).

To effectively manage neonatal and maternal mortality, as well as to significantly enhance public health, it is crucial to understand the primary causes of child's death rates. Therefore, policymakers and designers have produced guidelines to address these linked predictor factors with appropriate intervention in order to enhance the public health status of mothers and neonates. The sustainability of reducing the early neonatal mortality rate will be protected by developing appropriate guidelines and regulations (5). According to (6), Ethiopia is one of the top NMR contributors, ranking sixth overall and second in the SSA after Nigeria.

Some of the most predictor factors associated with neonatal mortality are sex of the neonate (7), Antenatal Care (ANC) visit(8, 9), birth weight (low birth weight) (8, 9), preterm birth, fetal growth restriction and congenital abnormalities (10). Therefore, professional delivery assistance, high-quality antenatal care, and postnatal care follow-up should be used to reduce the highest NMR of children and incidence of difficulties during the initial neonatal period and to ensure the survival of neonatal babies.

The baby and under-five mortality rates in Ethiopia show a consistent downward trend over the preceding 15 years. On the other hand, despite the fact that the NMR slightly dropped from 39 fatalities per 1000 total live births in 2005 to 29 total live births in 2016. As a result, this report demonstrates that it has continued to be a stable high. In comparison to the national average mortality rate of 30 deaths per 1000 pregnancies (11, 12), the Tigray national regional State has a higher NMR of 34 total deaths per 1000 pregnancies, according to the Ethiopia Demographic and Health Surveys (EDHS) 2016 data.

Ethiopia is one of the SSA nations that, as of 2015, had fulfilled the fourth Millennium Development Goal (MDG4) commitment to reduce the mortality rate of children under the age of five. Even if the death rate for children has significantly decreased. NMR, though, is still high across the nation. Therefore, a significant decrease in NMR is essential to further achieving this objective in the future. According to earlier research, early NMR has been declining more slowly than late NMR during the past three decades.

It is important to control the present health programs and establish policies on improving the current situation for mother and neonate health status, which is why interventions to reduce neonatal mortality are a major concern and belong to enhancing maternal public health care. Additionally, understanding the risk factors for newborn mortality is crucial for tracking the effectiveness of intense, scientifically supported public health measures to prevent neonatal deaths (13).

There have been numerous investigations into the risk factors for the mortality of children under the age of five in Ethiopia. There are, however, few researches that examine the NMR and the risk factors that go along with it. The majority of these studies are nation-level investigations. As the country result may not accurately reflect the situation at regional levels, such studies omit a crucial point for policymakers and designers (14, 15). We conducted an all-inclusive retrospective cross-sectional study design analysis of the most recent EDHS 2016 to address the aforementioned gap and identify the key risk factors for NMR in the Tigray Regional State, taking into account a variety of socioeconomic, demographic, and environmental factors (11). Therefore, the objective of this study was to assess the predictors of neonatal mortality in the Tigray region of northern Ethiopia.

Method

Source of data, study design, and period: On the basis of the EDHS 2016 dataset, a retrospective cross-sectional study design was used to perform this investigation. Between January and June of 2016, the Ethiopian Public Health Institute (EPHI), Central Statistics Agency, and Ministry of Health (MOH) performed the survey. It was sponsored from the United States Agency for International Development (USAID). This survey report's main goal is to provide policymakers and designers with comprehensive data on fertility, adult, newborn, child, and maternal mortality, maternal and child health status, nutrition, and knowledge of HIV/AIDS and other sexually transmitted illnesses.

Sample size determination technique and study population: Two stages of sample selection were used to implement this survey report's study design. There are 9 Regional States and 2 administrative cities in the nation. In the initial round, 645 enumeration areas 443 in rural and 202 in urban areas had been chosen with probability inversely correlated to size. In the second stage, the freshly constructed household list was systematically selected, with 28 households per cluster being selected with equal probability. All reproductive women between the ages of 15 and 49 who were stable residents of the chosen households and had spent at least one night there prior to the survey were eligible for the interview. Since the 2016 EDHS, a total of 15,683 women of reproductive age (15-49), 12,688 males of reproductive age (15-59), and 16,650 families have been questioned. 1,682 of these households came from the northern Ethiopian region of Tigray. In the five years before to the study, 4,428 live births were registered in the Tigray Regional State. The source population consisted of all neonates reported in the Tigray Regional State of Northern Ethiopia over the five years prior to the survey who were less than or equal to 28 days old. Next, using a sample selection procedure that is illustrated in Figure 1, newborns with completed records of information on neonatal death within the previous five years were found (11). Finally, samples of a total of 716 neonates who had full disclosure of all the risk factors taken into consideration were included.

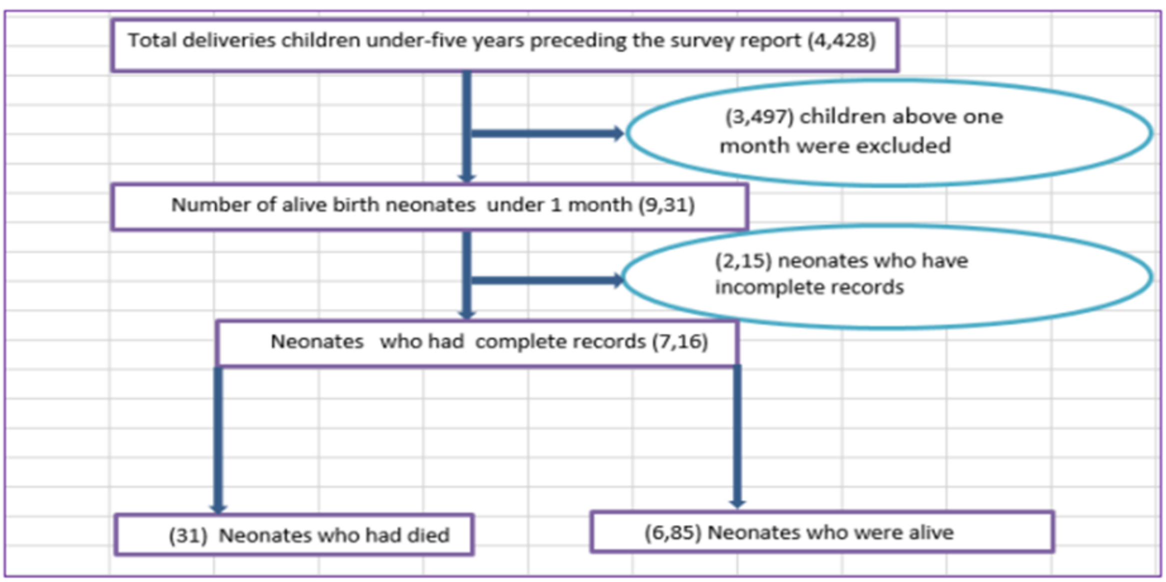

Figure. 1 Diagrammatic presentation of sample selection among neonates included in Tigray Regional State, Northern Ethiopia, 2016.

Study area: Tigray Region State is located between 36 and 40 degrees' East longitude North of Ethiopia bounded in the North with Eritrea, in the South Amhara Regional State, Sudan in the West and in the East Afar Regional State. According to the 2007 Ethiopian population and housing census survey, there were 3,136,267 people living in the Tigray Regional State, of which 1,542,165 were men. Around 2,667,789 people (or 85%) of the population lived in rural areas (16).

Variables of the study

Response variable: The response variable of this study was time to neonatal mortality of neonates which measured in days. In this study, "death" refers to a neonate who has passed away, whereas "censored" refers to neonate who is still living. The time from initial of observation until the occurrence of outcome of observation (death and censored i.e., assumed as right-censored). Then, neonatal mortality will be obtained from the death of live birth within 28 days of life (i.e., death of neonates between 1–28 days). Therefore, the outcome variable for the neonate is dichotomous, represented by a random variable that takes the value "1" with probability of success (had neonatal death) and the value "0" with probability of failure (were neonatal alive), such that

$$Y_i = \begin{cases} 1, \text{if } i^{th} \text{ neonate's had experinced with neonatal mortality (had died)}. \\ 0, \text{if } i^{th} \text{ neonate's had not experinced with neonatal mortality (were censored)}. \end{cases}$$

Independent variable: The explanatory variables were included in this study: mother's age (35 and above, 20-34, 19 and below), birth type of neonate (singletons, multiple), ANC visit (no, yes), sex of neonate (female, male), toilet facility using of mother's (with facility, no facility), place of delivery of neonate (health facility, home), residence place of neonates (rural, urban), drinking water source of mother's (protected, piped, unprotected), and exclusive breastfeeding (no, yes).

Statistical data analysis: Statistical analyses were performed using STATA version 14 statistical software (Appendix 1). For categorical predictor variables, Kaplan-Meier estimators were employed to show participant survival across time. The percentage and frequency distribution of the individuals in relation to all factors were described using descriptive statistics. Additionally, tables and figures were employed to present the data. In this study, five parametric survival models (i.e., Exponential, Weibull, Log-logistic, Lognormal and Gompertz) were fitted to identify the risk predictor factors of neonatal mortality. Using the Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), and Log-likelihood Information Criteria, the best model was chosen. The Wald test and Cox-Snell residual test were used to evaluate the goodness of fit test. Variables having P-value < 0.05 in the multivariable model were considered significantly associated with the response variable. To demonstrate the strength of the link, the adjusted hazard ratio (AHR) and its 95% confidence interval (CI) were computed.

Kaplan-Meier estimation: The Kaplan-Meier (K-M) curve is a nonparametric method used to estimate the survival experience. The survival experience of two or more groups of between-subjects factor can be compared for equality. It expressed as the survivor function of $S_{(t)}$.

$$S_{(t)} = \begin{cases} \prod_{t_j \le t} \left(1 - \frac{d_j}{n_j}\right), & t \ge t_1, \\ 1 \;, & 0 < t < t_1, \end{cases} \quad (1).$$

Where; , is the number of participants who experience the event at a time , and, is the number of participants.

Weibull regression survival model: The Weibull distribution provides as one of the most commonly used parametric survival models. It plays a central role in the analysis of survival time dataset. The probability density function of the Weibull distribution with scale parameter and shape parameter γ,W(λ, γ), can be expressed as W(λ, γ) = . The survivor and hazard functions of a W (λ, γ) distribution are given by the following respectively;

$$s(\lambda,\gamma) = exp[-(\lambda t)^{\gamma}] \quad (2).$$

$$h(\lambda,\gamma) = \lambda\gamma t^{\gamma-1} \quad (3).$$

Where; is denotes the hazard for an event for neonates, is denoted the survival of patients. This hazard model was used to investigate and to check the impact on each independent variable on mortality rate. If γ = 1, the hazard will be constant over time and hence is equivalent with the exponential survival time. If γ >1, the hazard increases with time and if γ < 1 the hazard decreases as time increases. The method of maximum likelihood estimator is used to find estimators of the parameters λ and γ.

Model selection criteria: In this study, some evaluation factors will be taken into account in order to choose the optimum parametric model for simulating participant survival. To have an appropriate model selection for the bi-variable and multivariable parametric survival models most commonly known model selection criterions; AIC and BIC were considered for this study.

$$AIC = -2 * ln(likelihood) + 2 * k \quad (4).$$

$$BIC = -2 * ln(likelihood) + ln(N) * k \quad (5).$$

Where; k is number of parameters estimated, N is total number of observations used to fit the model. The smallest statistic values of AIC and BIC reflect an overall best fit.

Result

Descriptive characteristics of study participants: In the cross-sectional study, there were 716 participants, and 31 (4.3%) of them died. 357 (49.9%) of the total participants were male, and 396 (55%) were born in a hospital or medical facility. Moreover, the majority of participants 697 (97%) of them were singleton type of births. From all, 435 (61%) of mother's age were 35 years and above. On the subject of education level, 93 (13%) of them were primary education complete, 236 (33%) of them were illiterate, and 387 (54%) were secondary and above education level. On the other hand, majority of participants 595 (83%) were done ANC visit (**Table 1**).

Table 1: Socio-demographic characteristics, health and environmental predictors of mothers and neonates in Tigray Regional State, Northern Ethiopia, 2016 (N = 716).

Variables	Categories	Frequency (N)	(%)
Mother's age	19 and below	36	5
	20-34	245	34
	35 and above	435	61
Birth type	Multiple	19	2.7
	Singletons	697	97
Sex of neonate	Male	357	50
	Female	359	50
ANC visit	Yes	595	83
	No	121	17
Toilet facility	No facility	372	52
	With facility	344	48
Mother's education level	Secondary and above	387	54
	Primary	93	13
	Illiterate	236	33
Residence	Urban	22	3.1
	Rural	694	97
Drinking water source	Unprotected	135	19
	Piped	179	25
	Protected	402	56
Place of delivery	Health facility	396	55
	Home	320	45
Exclusive breastfeeding	No	193	27
	Yes	523	73
	Total neonates	716	100

Neonatal mortality rate and time-to-death of neonates in Tigray Regional State, Northern Ethiopia: The neonates were followed up time for a minimum of 1 day to a maximum of 28 days. The cohort contributed a total of 7159 neonate-days. Study neonates were followed for an overall estimated mean follow up time of 10.0 days [95% CI: (9.67, 10.3)]. During this follow up time the mortality rate of neonates was found to be 4.3 neonatal death (95% CI: 2.8, 5.8) per 100 total live births which is equivalent to the NMR of 43 per 1000 total neonates with [95% CI: (28, 58)].

Comparison of the survival ability of participants: From the K-M survivor estimate, singletons birth type children and public health place of delivery had shortened survival time to mortality as compared to its counter parts (**Figures 2).**

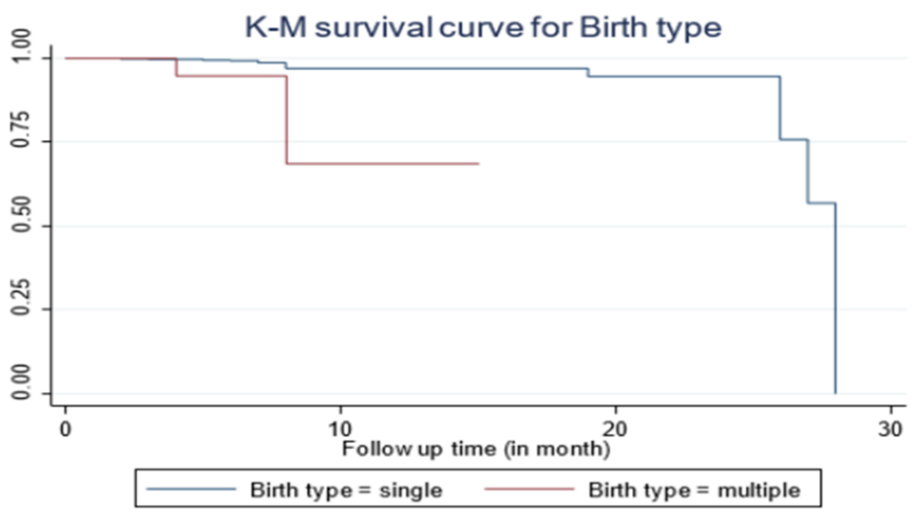

Figure 2. Kaplan-Meier survival curve for birth type in Tigray Regional State, Ethiopia

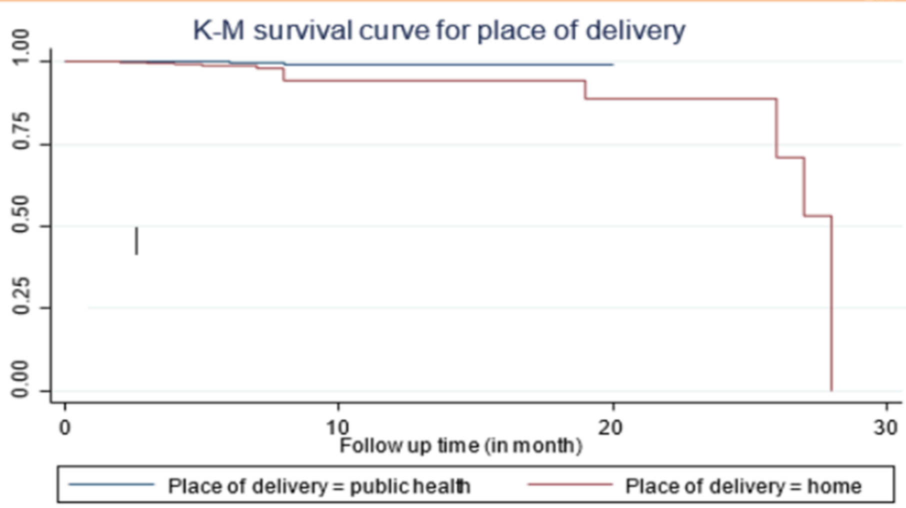

Figure 3. Kaplan-Meier survival curve for place of delivery in Tigray Regional State, Ethiopia

Model selection information criteria and goodness of fit model analysis results: The study compared various parametric survival models using the information criterion. The researchers employed the AIC and BIC model selection techniques for each model study. The value of AIC and BIC are computed as;

AIC = -2*ln(likelihood) + 2*k and BIC = -2*ln(likelihood) + ln(N)*k

Where; k = number of parameters estimated, N = number of observations.

According to the following statistics result of the AIC, BIC, and Log likelihood criteria the Weibull-regression parametric survival model was preferable for modelling since the lowest value is preferable. Therefore, the Weibull-regression model was done for a more accurate identification of the major risk predictors for neonates. This indicates that in terms of relative efficiency and parameterization the Weibull model is the best efficient for predicting survival of neonates (Table 2). Similarly, the survival probability plot of the five parametric survival models stated indicates that the Weibull distribution implements better because it displays a clear step function than the other distributions and this also justifies the result value of AIC and BIC (**Figure 4**). Moreover, the authors checked the overall goodness of fit model done by the Wald test and Cox -Snell residual test. Therefore, the Wald test provided a chi-square value of 188.6 with 13 degrees of freedom and p-value < 0.001, which would imply that a good fit for the model (**Table 3**). Correspondingly, Cox-Snell residual test was used to check the goodness of model fitness. This graph shows that the hazard function follows the 45^{o} closed to the baseline (**Figure 5**).

Table 2: Selection of the best fitted models for neonatal mortality data in Tigray Regional State, Northern Ethiopia, 2016.

	Models			
Information Criteria	**Weibull**	Gombertz	Log logistic	Lognormal
AIC	**199.04**	201.8	203.3	210.3
BIC	**267.6**	270.4	271.9	278.9
Log-likehood	**-84.5**	-85.9	-86.7	-90.16

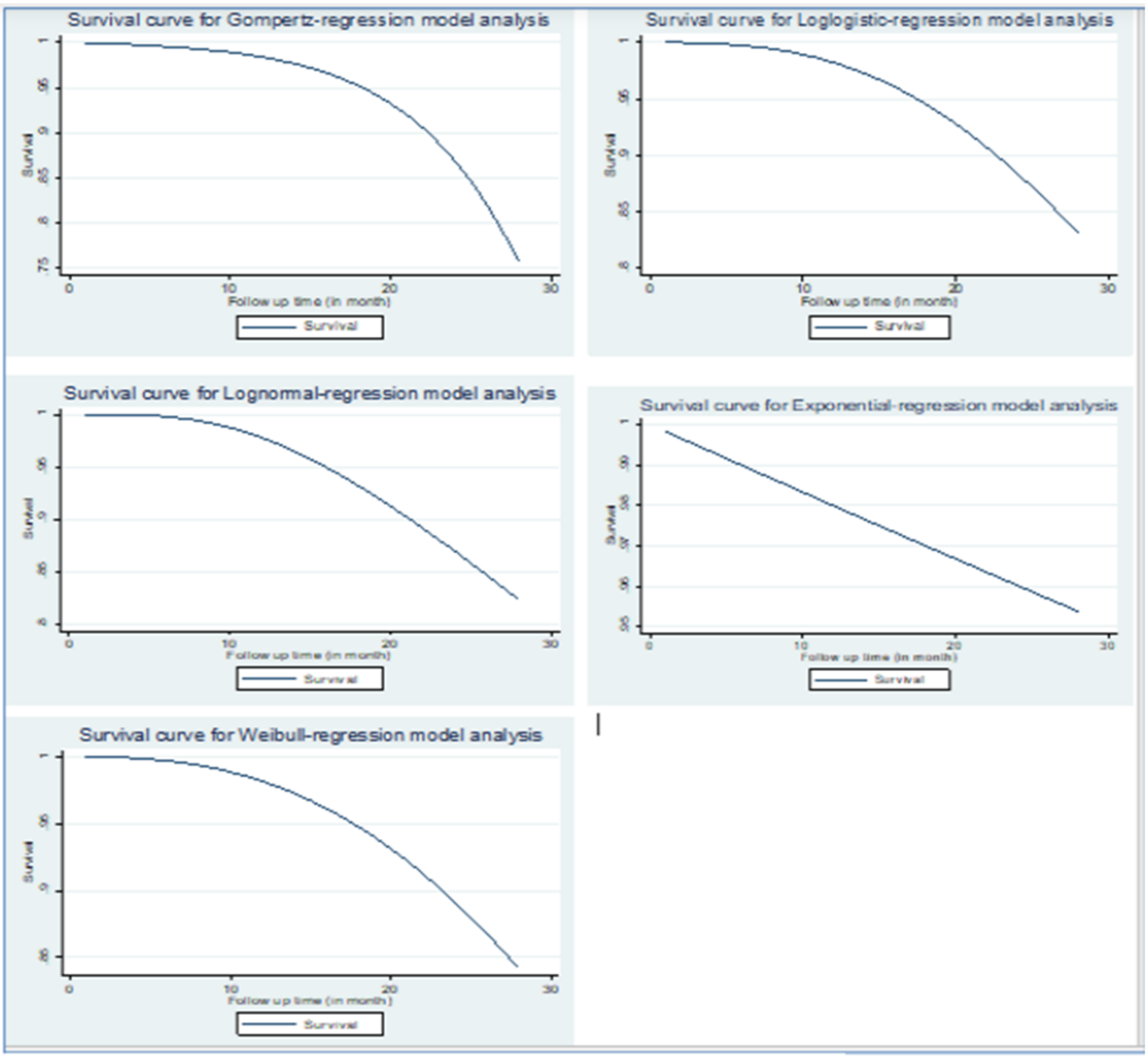

Figure 4. ***Survival plot of the five parametric survival models***

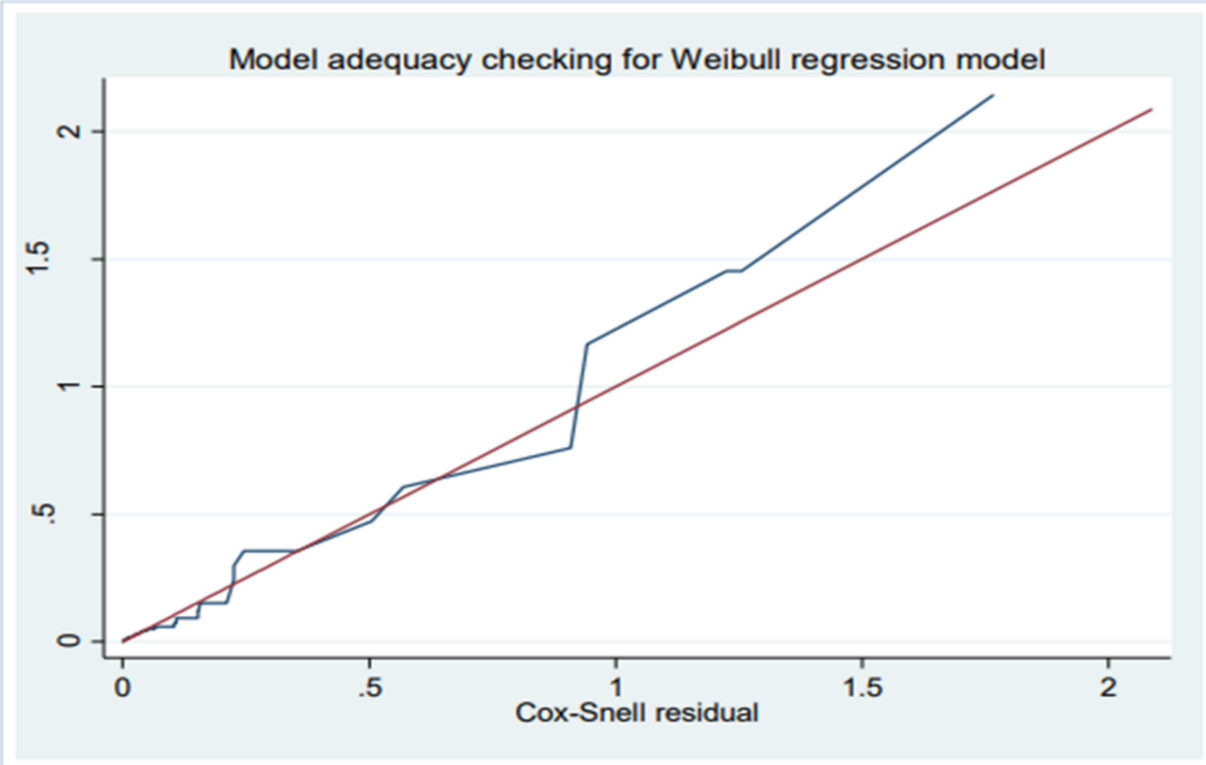

Figure 5: Cox-Snell residual Nelson-Aalen cumulative plots to assess model fitness of the Weibull regression model in Tigray Regional State, Northern Ethiopia.

Predictor factors of neonatal mortality in the Tigray Regional State, Northern Ethiopia

Weibull regression model analysis: Weibull-regression model analysis was done to identify the effect of each predictor variables on the neonatal mortality.

Predictor of neonatal mortality rate: Both bi-variable and multivariable Weibull-regression model analysis of risk factors associated with neonatal mortality was presented in **Table 3**. From the bi-variable model analyses; birth type, sex of neonate, residence, exclusive breastfeeding, and place of delivery were significant predictors of neonatal mortality among neonates in the Tigray Regional State. After adjusting for other predictor variables the result showed that; birth type and place of delivery were statistically significant predictors of neonatal mortality. However; mother's age, exclusive breastfeeding, sex of neonate, ANC visit, toilet facility, mother's education level, residence, and drinking water source were not statistically significant. According to the results from **Table 3**, the hazards of neonatal mortality rate were higher among neonates that were multiple (AHR = 10.9, 95% CI: 3.4, 35.5) than those in singletons births.

Concerning place of delivery, the hazards of neonatal mortality rates were higher among neonates with those who did not used health facility during birth (at home) (AHR = 10.5, 95% CI: 3.0, 36.6) compared to that of with health facility. The scale parameter of the Weibull-regression model was found to be $\gamma = 2.6$[95% CI: (2.1, 3.4)]. This interval doesn't include $\gamma = 1.0$ suggesting that the Weibull-regression model analysis is more appropriate than the other parametric survival models. Since $\gamma = 2.6$ which is greater than 1, the hazard of experiencing neonatal mortality decreases as survival time increases (see **Table 3**).

Table 3: Predictors of neonatal mortality using Weibull-regression model analysis in the Tigray Regional State, Northern Ethiopia, 2016 (N = 716).

	Survival status		Bivariable analysis	Multivariable analysis
Variables	**Died (death=1)**	**Censored (censored=0)**	**CHR (95% CI)**	**AHR (95% CI)**
Mother's age (ref.= 19 and below)	1	35		
20-34	21	224	5.1 (0.68, 37.7)	2.17 (0.28, 17.1)
35 and above	9	426	0.76 (0.1, 6)	0.48 (0.06, 3.9)
Birth type (ref.= singletons)	25	672		
Multiple	6	13	14.8 (5.9, 36.9)*	10.9 (3.4, 35.5)*
Sex of neonate (ref.= female)	7	352		
Male	24	333	2.9 (1.25, 6.76)*	2.2 (0.89, 5.2)
ANC visit (ref.= no)	9	111		
Yes	22	574	0.74 (0.34, 1.6)	1.7 (0.45, 6.1)
Toilet facility (ref.= with facility)	14	330		
No facility	17	355	1.2 (0.58, 2.4)	1.6 (0.54, 4.6)
Mother's education level (ref.= illiteracy)	15	221		
Primary	1	92	0.23 (0.03, 1.7)	0.18 (0.02, 1.6)
Secondary and above	15	372	0.8 (0.39, 1.6)	0.38 (0.13, 1.1)
Residence (ref.= rural)	29	665		
Urban	2	20	4.8 (1.10, 20.6)*	0.77 (0.13, 4.5)
Drinking water source (ref.= protected)	18	384		
Piped	9	170	0.82 (0.37, 1.8)	
Unprotected	4	131	0.66 (0.22, 1.9)	1.3 (0.42, 4.1)
Place of delivery (ref.= health facility)	3	317		
Home	28	368	10.1 (10.1, 33.1)*	10.5 (3.0, 36.6)*
Exclusive breastfeeding (ref.= no)	17	179		
Yes	14	506	2.4 (1.2, 4.8)*	1.3 (0.59, 2.8)
Cons			------------	0 (0, 0.0002)*
/ln_p			------------	0.97 (0.73, 1.2)
P = γ			------------	2.6 (2.1, 3.4)*
1/p = □			------------	0.38 (0.299, 0.48)*

Discussion

This study was conducted to assess predictor factors of NMR among neonates in the Tigray regional state, northern Ethiopia. The 2016 EDHS indicated that NMR is still one of the leading causes of illness and mortality among neonates. The magnitude of NMR is greater than the national average, and the early neonatal period has been associated with the highest chance of newborn mortality. Neonates whose mothers gave birth at home and who belonged to the child multiple birth type had a higher risk of NMR. In the current study, the overall neonatal mortality rate among neonate children was 4.3% which is equivalent to the NMR of 43 per 1000 live birth neonates with [95% CI: (28, 58)]. This finding confirms with the study done in Indonesia, 5.2% (17), Nigeria, 4.1% (8), Somali region of Ethiopia, Jimma Zone, 3.55% (18), and Ethiopia, 3.67% (19).

The outcome of this study, however, was less favorable than that of the research carried out at the University of Gondar Comprehensive Specialized Hospital in Northwest Ethiopia, 17.3% (6), WolaitaSodo Referral Hospital in southern Ethiopia, 17.3% (20), Debre Markos Referral Hospital in Northwest Ethiopia, 21.3% (21), and Amhara Regional State Referral Hospitals, Ethiopia, 18.6% (6).

On the other hand, it was more than the study done in China, 1.2% (22), and rural area of Eastern Ethiopia, 2.84% (23). This difference might be attributed to variation in study design, study settings, follow-up period, population sample size of the study, and socio-demographic characteristics of study participants.

The mother's age was identified as a significant risk factor for newborn mortality in a number of published publications. This study, however, demonstrated that the mother's age had little bearing on infant death. This is inconsistent with findings from other studies (2). Unlike other studies, male sex of neonate, not ANC visit and not initiating exclusive breastfeeding, and rural place of residence weren't responsible risk factors of neonatal mortality (2, 6, 7, 24).

Place of delivery was discovered to be a significant risk factor for neonatal mortality, meaning that babies born at home had higher risks of dying than babies who received care in health institutions. Prior, studies also reported that neonates who born in health facilities had better access to delivery services and better health care services for health service utilization for their newborn (6; 25).

One of the risk variables affecting a newborn's chance of survival is their birth type, which might vary depending on their socio-demographic parameters. Multiple births have a higher risk of infant mortality than single births. This study was similar with the previous studies done in Ethiopia (2). The cause may be explained by the fact that neonates from multiple births are more likely to have low birth weight and biological immaturity.

Limitation and strength of the study: This inquiry pinpointed the NMR issue inside the research domain. However, it is important to consider some of the restrictions. The authors were unable to include some of the significant predictor variables that have been identified as linked risk predictors in this analysis because of the secondary retrospective nature of the dataset and the high rates of missing datasets for predictor variables. It's unclear how useful these results are (given the omission of some of the historically significant datasets) and that the associated predictors examined were a convenience sample of the dataset gathered as part of the DHS. Also, the study was completed eight years ago. Therefore it is unlikely to accurately reflect the most recent developments about NMR in the region. Additionally, it was predicated on a suitable statistical model technique (parametric analytic comparison) to forecast the majority of risk factors for newborn mortality. Besides, because the study is according to the regional survey information, it may provide insight into how policymakers and program planners should develop effective regional intervention methods.

Conclusion

The prevalence of NMR showed that the NMR in the Tigray region was greater than the national average. The current study identified the multiple birth type and home delivery of the neonates as crucial predictor factors for NMR. Interventions should be improved to these modifiable major predictor factors that significantly decrease the NMR problem among neonates.

Abbreviations:
ANC; **A**ntenatal **C**are; AHR: **A**djusted **Hazard**s **R**atio; CI: **C**onfidence **I**nterval; CSA: **C**entral **S**tatistical **A**gency; EDHS: **E**thiopian **D**emographic **H**ealth **S**urvey; EPHI; **E**thiopian **P**ublic **H**ealth **I**nstitute;MDG4: **M**illennium **D**evelopment **G**oal; MOH: **M**inistry of **H**ealth; NMR: **N**eonatal **M**ortality **R**ate; UNICEF: **U**nited **N**ations **I**nternational **C**hildren's **E**mergency **F**und; USAID: **U**nited **S**tates **A**gency for **I**nternational **D**evelopment; SSA: **S**ub-**S**aharan **A**frica.

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