

Time to Death and Predictors Among Neonates with Neural Tube Defects in Two Public Hospitals, Addis Ababa, Ethiopia: A Retrospective Follow-Up Study

Ezedin Mohammed Hiyar¹, Girum Sebsibie Teshome², Feven Mulugeta Ashagre³, Solomon Hailesilassie Bisrat⁴, Terefe Keto⁵, Mehuba Hassen Ali⁶

¹Department of Nursing, Dilla University, Dilla, Ethiopia; ²Department of Pediatrics, University of Rwanda, Kigali, Rwanda; ³Department of Nursing, Addis Ababa University, Addis Ababa, Ethiopia; ⁴Department of Surgery, University of Gondar, Gondar, Ethiopia; ⁵Department of Nursing, Mizan Aman Health Science Colleges, Mizan-Aman, Ethiopia; ⁶Department of Nursing, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

Correspondence: Girum Sebsibie Teshome, Department of Pediatrics, University of Rwanda, Kigali, Rwanda, Email girumseb@gmail.com; Ezedin Mohammed Hiyar, Department of Nursing, Dilla University, Dilla, Ethiopia, Email ezedin49@gmail.com

Background: Neural tube defects are a collection of intricate congenital abnormalities that affect the central nervous system. Neural tube defects cause 88,000 deaths globally and 29% in developing countries. Neural tube defects take a significant portion of the congenital anomalies in Ethiopia. This study aimed to assess the time to death, as hazard and predictors among neonates with neural tube defects in two public hospitals, Addis Ababa, Ethiopia.

Methods: A retrospective cohort study was conducted by reviewing medical charts of 410 randomly selected neonates with neural tube defects, registered from 2018 to 2022 in Addis Ababa, Ethiopia. Data collection and entry was done from February 20 to March 20/2023 using KoboCollect v2022.4.4. STATA/14 was used for data screening, and SPSS/27 was used for analysis. The Kaplan-Meier survival analysis and Cox proportional hazards model were used for inferential analysis. Findings with $p \leq 0.05$ were observed as statistically significant.

Results: A total of 410 neonates were followed for 4100 person-days of risk time and 35 (8.54%) of neonates expired. The overall incidence rate of mortality was 8.54 per 1000 neonate days of observation with a median survival time of 25 days (95% CI: 22.7–27.3). Being preterm, Adjusted Hazard Ratio (AHR) = 2.62, (95% CI 1.12, 6.14), having low birth weight (AHR: 2.62, 95% CI 1.13, 6.10), encephalocele (AHR: 3.77, 95% CI 1.65, 8.62), cervical and occipital lesion level (AHR: 3.97, 95% CI, 1.17, 13.49), presence of hydrocephalus (AHR: 3.98, 95% CI 1.55, 10.21), and Chiari-II malformation (AHR: 2.40, 95% CI 1.03, 5.57) were demonstrated to be statistically significant predictors of time to death.

Conclusion: The cumulative incidence of death of neonates diagnosed with neural tube defects was observed. Early diagnosis and timely management of patients is decisive in lowering the mortality.

Keywords: neural tube defects, time to death, Addis Ababa, Ethiopia

Introduction

Neural tube defects (NTDs) are a diverse and intricate group of congenital malformations of the brain, spine, and spinal cord, resulting from the failure of neural tube closure during embryogenesis.^{1,2} They are one of the most common and most severe congenital anomalies.³ NTDs are believed to be caused by a number of genetic, environmental, and dietary factors, while the exact cause is yet unknown.⁴ The majority of open NTDs are immediately noticeable at birth, whereas closed NTDs are generally asymptomatic and diagnosed incidentally.^{5,6} The pathogenesis of most of the NTDs is thought to stem from a primary failure of the embryonic neural tube to close. Nevertheless, there is some strong clinical and experimental evidence in favor of the idea that a closed neural tube could subsequently reopen and cause NTDs.^{2,7}

Despite advancements in neonatal care, neonates with neural tube defects (NTDs) continue to face high mortality rates, especially in low-resource settings like Ethiopia. Although Addis Ababa has relatively better health infrastructure

than others in the regions of Ethiopia, there is limited evidence on the time to death and its predictors among these neonates, hindering timely and targeted interventions. Most existing studies focus on prenatal risk factors and surgical outcomes, leaving a gap in understanding postnatal survival and mortality determinants.⁵ This study aims to fill that gap by identifying when and why these deaths occur, thereby supporting improvements in neonatal care and follow-up. Addressing this issue aligns with global health priorities, particularly Sustainable Development Goal 3, which targets the reduction of neonatal mortality, and Ethiopia's national health strategies that prioritize early detection and management of birth defects. By providing critical insights into mortality patterns, this research supports informed policy and clinical decision-making to reduce preventable deaths among neonates with NTDs.³

Globally, NTDs affect 320,904 infants and account for 0.5–2 per 1000 pregnancies.^{8,9} The combined prevalence of all NTDs in Eastern Africa was 33.30 per 10,000 live births, and the highest NTD birth prevalence was found in Ethiopia (60 per 10,000).¹⁰ Also, NTDs are responsible for 88,000 yearly fatalities besides leaving 8.6 million people with disabilities, and they account for 29% of neonatal mortality in developing countries, Ethiopia having 41% proportion death of NTDs. The probability of survival of infants with NTDs in developed countries found to be around 96%. However, it is significantly lower in developing countries having a long-term survival probability of 55%.^{9,11}

NTDs are considered a significant contributor to perinatal morbidity and mortality, as they may cause spontaneous abortion, stillbirth, and early neonatal death from CNS (Central Nervous System) infections, or to lifelong crippling disabilities, ranging from lower paralysis and loss of sensation to stool and urine incontinence, hydrocephalus (58%), Chiari malformation (50.6%), mental, and physical retardation.^{12–17}

Furthermore, numerous children who survive also deal with a variety of serious social, neurocognitive, emotional, self-esteem, psychiatric, and economic issues, which not only affect individuals but also place a heavy strain on society as a whole.^{18,19} Due to the lack of adequate rehabilitation facilities in Sub-Saharan Africa (SSA), the effects of debilitating malformations are more severe, and these morbid and fatal defects account for a significant portion of the congenital anomalies observed in Ethiopia.^{1,16}

Neonatal mortality and NTDs case fatality can be decreased by folic acid food fortification, peri-conception folic acid supplementation and providing quality medical and surgical care.^{20,21} The strongest risk factors for a rise in the case fatality of newborns with NTDs include preterm delivery and low birthweight, hence it is essential to pay special attention to these vulnerable infants.^{22,23}

Considering the morbidity and mortality, knowing the particular time which pose a risk of death among neonates with NTDs is vital for health care providers, policy makers and other stakeholders to act timely and accordingly. Also, factors associated with death should be identified with regard to time for prevention and management of NTDs cases. Despite this, there are hardly any studies on the time to death and predictors among neonates with neural tube defects, not just in Ethiopia but also globally.

In order to close this gap and help develop guidelines for preventing neonatal mortality from neural tube defects, the study will estimate the median time to death and identify predictors of mortality among neonates with neural tube defects admitted to Zewditu Memorial Hospital and St. Peter's Specialized Hospital. This will help the country to achieve its 2030 Sustainable Development Goals (SDGs), which include lowering child mortality and promoting health equity.

Methods and Material

Study Design, Area, and Period

A retrospective follow-up investigation was carried out at the study hospitals from November 2022–June 2023 based on a medical record review of Neural tube defect patients registered from January, 1 2018 to December, 31 2022. The study was conducted at Zewditu Memorial Hospital and St. Peter's specialized Hospital in Addis Ababa, the capital city of Ethiopia. These hospitals are currently serving as the two major public neurosurgical centers in the country.

Study Population

All neonates diagnosed with neural tube defects who were admitted to Zewditu Memorial Hospital and St. Peter's specialized Hospital from January, 1 2018 to December, 31 2022. Charts of neonates with incomplete information and not available during data collection were excluded.

Determining the Sample Size and the Sampling Process

Sample Size Determination

The sample size was calculated by using single population proportion formula, taking $Z_{\alpha/2}$, 1.96 at 95% C.L., Margin of error (d), 0.05, and 41% for proportion of death of neural tube defect cases from a study conducted in Ethiopia.¹¹ Thus, the total sample size determined after adding 10% contingency for possible missed data was 410.

Sampling Procedure

The two major governmental neural tube defects management hospitals in Addis Ababa were purposely selected. The selected hospitals were Zewditu Memorial Hospital and Saint Peter's Specialized Hospital. Five consecutive years of data; from Jan.,1 2018 to Dec.,31 2022 were included. During the five years period, the total number of neural tube defect admission (N) was 1,315 (Z.M.H, $N_1=1,048$ and St. P.S.H $N_1=267$).

The total sample size (410) is proportionally allocated, Eqn for the recruitment years (2018, 2019, 2020, 2021 and 2022) based on their contribution to the total number of admitted NTD cases in each hospital. The sampling interval (K) is 3, and it is similar for each hospital. A systematic random sampling technique was used. (Figure 1)

Operational Definitions

Event: Is considered to be the death of neonates with neural tube defects while in the hospital and was recorded. Time to death: The follow-up of time from diagnosis to the occurrence of death. Censored: Refers to neonates with neural tube defects, who left the follow-up without having the event. Neural tube defects: Cases with confirmed radiological evidence and/or overt clinical finding and documented on the chart as NTDs.

Data Collection Tool and Procedure

A data extraction tool was developed by reviewing the neurologic clinic follow-up chart and different related articles. The data extraction tool was prepared in English to extract all the relevant data from the patients' medical record. The tool consists of the socio-demographic and neonatal characteristics: maternal related characteristics: clinical-related characteristics and treatment-related characteristics.

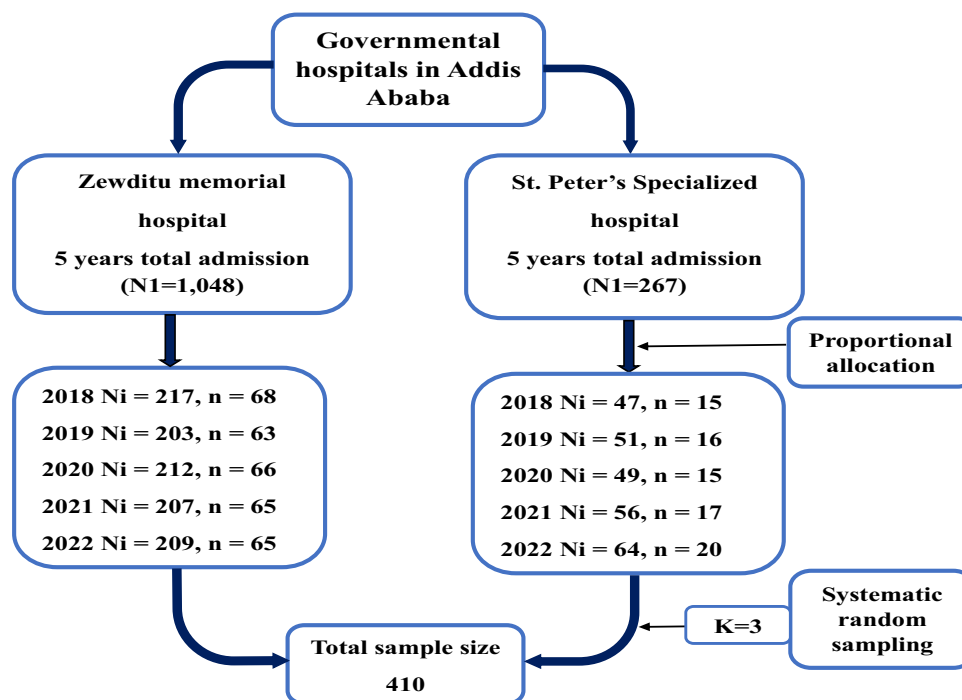


Figure 1 A sampling framework of time to death and its predictors among neonates with NTDs.

Medical record number of all charts of neonates with NTDs admitted to the study hospitals from January, 1 2018 to December, 31 2022, was retrieved from the registration books, and the charts of all study participants were selected based on the inclusion criteria.

Data Quality Control

The data extraction tool was checked for validity and reliability. Two data collectors and one supervisor were engaged in the data collection. Pre-test was done on 18 (5%) randomly selected charts at Zewditu Memorial Hospital, and these charts were not included in the actual data collection. The completeness and consistency of the collected data was checked daily during and after data collection, as well as at the time of cleaning, and analysis. The completed data extraction tool was cross-checked against the source data whenever there was incompleteness and ambiguity in recording. Records with incomplete data were excluded.

Dependent and Independent Variables

The dependent variable was time to death in days. Variables including gestational age, birth weight, multiple birth, maternal age, gravidity, folic acid intake, Hydrocephalus, lesion level, type of variant, associated congenital anomalies, Chiari-II malformation, motor function deficit, central nervous system infection and sepsis, time of surgical repair, surgical repair related complications and length of follow-up were considered as predictor variables.

Data Processing and Analysis

After the completion of data collection, cleaning and sorting was done using STATA software Version 14, then it was exported to SPSS version 27 for analysis. A preliminary analysis of the data was done to look for multicollinearity, potential outliers, and levels of missing values. The frequency, percentage, and rate were computed using descriptive statistics. The median was computed following a review of the data's distribution. To estimate the probabilities of death over time, a life table was constructed. Kaplan–Meier failure estimate curve was used to show the overall cumulative probability of failure, and Log rank test was done to compare the failure estimates of sub-variables of the covariates.

Cox regression models, both bivariate and multivariate, were employed for analysis. To determine the independent determinants of death, covariates from the bivariate Cox regression analysis with a P-value < 0.25 were fitted to the multivariate Cox regression analysis. All statistical tests were deemed significant at $P < 0.05$. By employing graphical (log-log plot) and statistical (Schoenfeld residuals) tests to verify proportional hazard assumptions, the Cox regression model's fit to the data was guaranteed. At the end, the results were summarized and presented using text, tables, and figures.

Results

Socio-Demographic Characteristics of the Study Participants

The study included 410 neonates with NTDs. More than half, 215 (52.4) out of 410 neonates, were males. The gestational age at admission ranged from 31 to 42 weeks with mean gestational age of 38.35 weeks ($SD \pm 1.78$) and 366 (89.3%) of them were born at term. The mean birth weight was 2917 gram ($SD \pm 515$). Of the cases, 76 (18.5%) were diagnosed prenatally. Almost all 398 (97.1%) of neonates were born singleton and 349 (85%) were referral cases. Most 380 (92.7%) of mothers age was ranged from 18 to 35 years. About 344 (83.9%) of the mothers gave birth via vaginal delivery and nearly all 396 (96.6%) of delivered at a health facility (Table 1).

Treatment and Clinical Characteristic of Neonates with Neural Tube Defects

Related to clinical characteristics, 196 (47.8%) of the neonates had hydrocephalus and 239 (58.3%) had motor function deficit. The most common type of variant, and lesion level of neural tube defects were found to be meningomyelocele 242 (59.0%) and sacral and lumbar lesion 163 (39.8%), respectively. Surgical repair was done for 328 (80%) neonates and 68 (16.6%) of them underwent surgical repair in less than 48 hours of birth. About 37 (11.3%) had a surgical repair related complication and 170 (64.6%) had a follow-up visit of one week. Out of all study subjects, 375 (91.46%) were censored, the remaining 35 (8.54%) were died. More than half, 68.5% of the participants have no radiological Chiari malformation (Table 2).

Table 1 Socio-Demographic Characteristics of Neonates Diagnosed with Neural Tube Defects in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410)

Variables	Category	Status		Total, n (%)
		Died n (%)	Censored n (%)	
Region	Addis Ababa	23(11.3)	181(88.7)	204(49.8)
	Oromia	11(8.5)	118(91.5)	129(31.4)
	Amhara	1(1.6)	62(98.4)	63(15.4)
	Others	0(0.0)	14(100.0)	14(3.4)
Admission source	In born	14(23.0)	47(77.0)	61(14.9)
	Out born	21(6.0)	328(94.0)	349(85.1)
Sex	Male	16(7.4)	199(92.6)	215(52.4)
	Female	19(9.7)	176(90.3)	195(47.6)
Gestational age	28-36 Week	20(24.4)	62(75.6)	82(20.0)
	37-42 Week	15(4.6)	313(95.4)	328(80.0)
Birth weight	1500-2499	26(24.8)	79(75.2)	105(25.6)
	≥2500	9(3.0)	296(97.0)	305(74.4)
Multiple birth	Singleton	34(8.5)	364(91.5)	398(97.1)
	Twins	1(8.3)	11(91.7)	12(2.9)
Time of diagnosis	Prenatal	7(9.2)	69(90.8)	76(18.5)
	Postnatal	28(8.4)	306(91.6)	334(81.5)
Maternal age	<18 Year	1(14.3)	6(85.7)	7(1.7)
	18-35 Year	31(8.2)	349(91.8)	380(92.7)
	>35 Year	3(13.0)	20(87.0)	23(5.6)
Folic acid supplementation	Yes	1(4.3)	22(95.7)	23(5.6)
	No	34(8.8)	353(91.2)	387(94.4)
Gravidity	Primigravida	12(8.8)	125(91.2)	137(33.4)
	Multigravida	23(8.4)	250(91.6)	273(66.6)
Place of delivery	Home	2(14.3)	12(85.7)	14(3.4)
	Health facility	33(8.3)	363(91.7)	396(96.6)
Mode of delivery	Vaginal delivery	28(8.1)	316(91.9)	344(83.9)
	Cesarean section	7(10.6)	59(89.4)	66(16.1)

Overall Survival of Neonates with Neural Tube Defects

The total follow-up period was 4100 neonatal days of risk time. For every 1,000 days that neonates with neural tube defects observed, about 8.54 deaths occurred. With a minimum follow-up period of one hour and a maximum follow-up period of twenty-eight days, the median time to death for the total cohort was twenty-five days, and the median follow-up

Table 2 Clinical Characteristics of Neonates Diagnosed with Neural Tube Defects Admitted in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410)

Variables	Category	Status		Total n (%)
		Died n (%)	Censored n (%)	
Hydrocephalus	Yes	22(11.2)	174(88.8)	196(47.8)
	No	13(6.1)	201(93.9)	214(52.2)
Lesion level	Sacral and Lumbar	4(2.5)	159(97.5)	163(39.8)
	Thoracic and Thoraco-lumbar	13(8.5)	140(91.5)	153(37.3)
	Cervical and Occipital	18(19.1)	76(80.9)	94(22.9)
Type of variant	Meningomyelocele	16(6.6)	226(93.4)	242(59.0)
	Meningocele	3(3.3)	87(96.7)	90(22.0)
	Encephalocele	16(20.5)	62(79.5)	78(19.0)
Associated congenital anomalies	Yes	12(10.4)	103(89.6)	115(28.0)
	No	23(7.8)	272(92.2)	295(72.0)
Chiari-II malformation	Yes	21(16.3)	108(83.7)	129(31.5)
	No	14(5.0)	267(95.0)	281(68.5)
Motor function	Yes	28(11.7)	211(88.3)	239(58.3)
	No	7(4.1)	164(95.9)	171(41.7)
Sepsis	Yes	21(20)	84(80)	105(25.6)
	No	14(4.6)	291(95.4)	305(74.4)
Meningitis (CNS infection)	Yes	4(7.3)	51(92.7)	55(13.4)
	No	31(8.7)	324(91.3)	355(86.6)
Surgical Intervention	Yes	21(6.4)	307(93.6)	328(80)
	No	14(17.1)	68(82.9)	82(20)
Time of surgical repair (n = 328)	≤48 Hour	8(11.8)	60(88.2)	68(16.6)
	>48 Hour	13(5.0)	247(95.0)	260(83.4)
Surgery related complications (n = 328)	Yes	4(10.8)	33(89.2)	37(11.3)
	No	17(5.8)	274(94.2)	291(88.7)
Duration of follow up visit (n = 263)	One Week	7(4.1)	163(95.9)	170(64.6)
	Two Week	3(4.5)	63(95.5)	66(25.1)
	>Two Week	1(3.7)	26(96.3)	27(10.3)

period was nine days. At the conclusion of the first, third, seventh, twenty-first, and follow-up periods, the cumulative chance of survival was 0.25%, 1.0%, 2.36%, 31.3%, and 74.5%, respectively (Figure 2).

Log rank test was done to compare the probability of hazard of time to death among different sub variables (Table 3). Accordingly, there was a significant difference ($P < 0.05$) in the median time to death of gestational age of 28–36 week and 37–42 weeks, with a median time to death of 21 and 27 days, respectively (Figure 3).

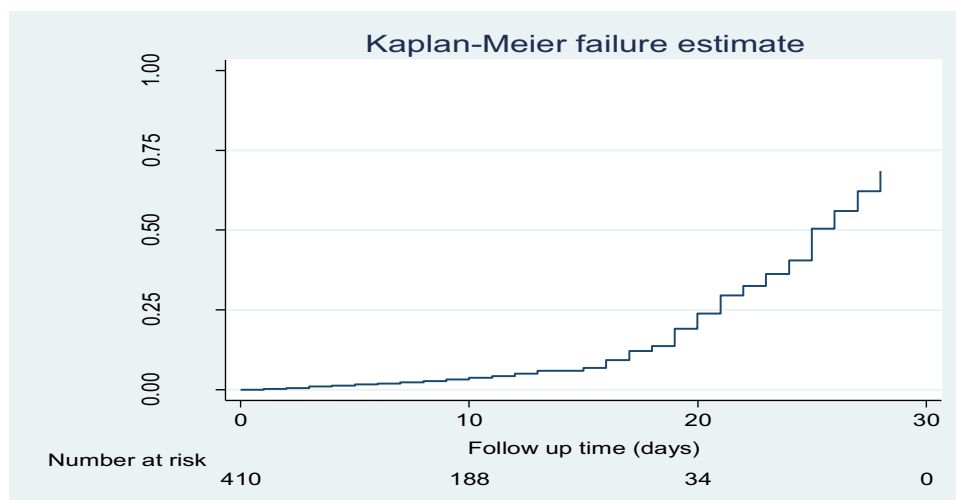


Figure 2 Kaplan-Meier failure estimate of time to death among neonates diagnosed with neural tube defects in Addis Ababa, Ethiopia, 2022 (n = 410).

The median time to death for neonates who low birth weight was 20 days and in those with normal birth weight and above was 28 days (Figure 4).

Moreover, the median time to death for neonates who had encephalocele was 23 days and in those with meningo-myelocele was 25 days (Figure 5). In addition, the median time to death for neonates who had Cervical and Occipital,

Table 3 Survival Time and Log Rank Test for the Sample Population Among Different Characteristics of Neonates with Neural Tube Defects in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410)

Variables	Category	Median Survival Time in Days (95% CI)	Log RankX2 Value	P-value
Gestational age	28-36 Week	21(17.83–24.17)	25.99	0.001
	37-42 Week	27(24.47–29.53)		
Birth weight	1500-2499	20(18.27–21.73)	29.76	0.001
	≥2500	28(24.27–31.73)		
Type of NTD	Meningomyelocele	25(21.31–28.69)	16.14	0.001
	Meningocele	-		
	Encephalocele	23(17.8–28.2)		
Lesion level	Sacral and Lumbar	-	23.48	0.001
	Thoracic and Thoraco-lumbar	25(19.92–30.08)		
	Cervical and Occipital	20(16.2–23.8)		
Hydrocephalus	Yes	24(18.9–29.09)	10.99	0.001
	No	26(21.51–30.49)		
Chiari-II malformation	Yes	23(20.45–25.56)	12.20	0.001
	No	27(24.51–29.49)		

(Continued)

Table 3 (Continued).

Variables	Category	Median Survival Time in Days (95% CI)	Log RankX2 Value	P-value
Sepsis	Yes	23(18.60–27.45)	8.49	0.004
	No	26(22.65–29.35)		
Motor function deficit	Yes	25(21.8–28.19)	5.68	0.017
	No	28(22.24–33.76)		

and Thoracic and Thoraco-lumbar lesion level was 20 and 25, respectively (Figure 6). The median time to death was significantly different for neonates with hydrocephalus and those free of hydrocephalus, having a median time to death of 24 and 26 days, respectively. The median time to death for neonates who had Chiari-II malformation was 23 days and in those without Chiari-II malformation was 27 days.

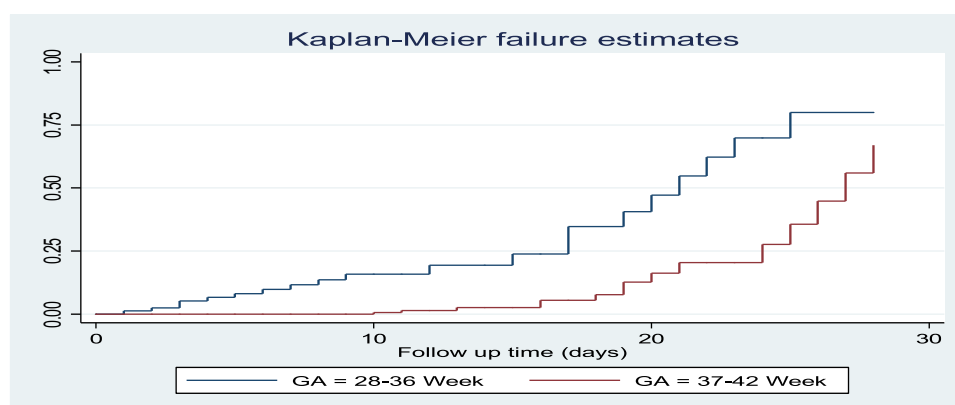


Figure 3 The Kaplan-Meier failure estimates of time to death, with categories of gestational age among neonates with neural tube defects in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410).

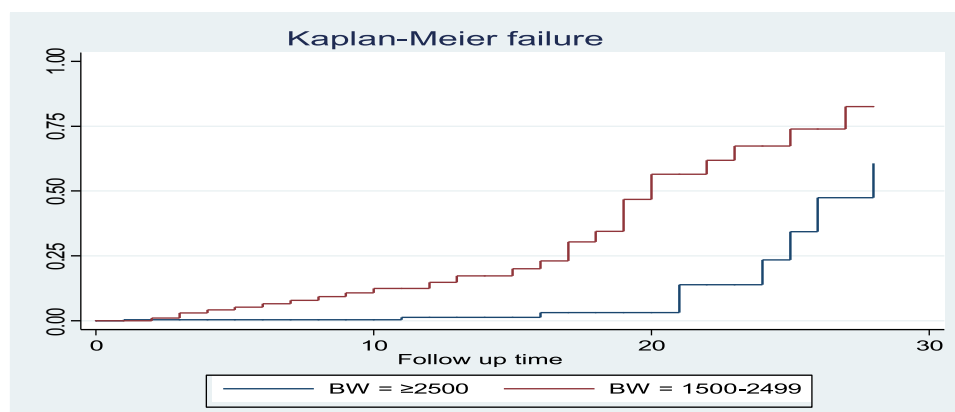


Figure 4 The Kaplan-Meier failure estimates of time to death, with categories of birth weight among neonates with neural tube defects in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410).

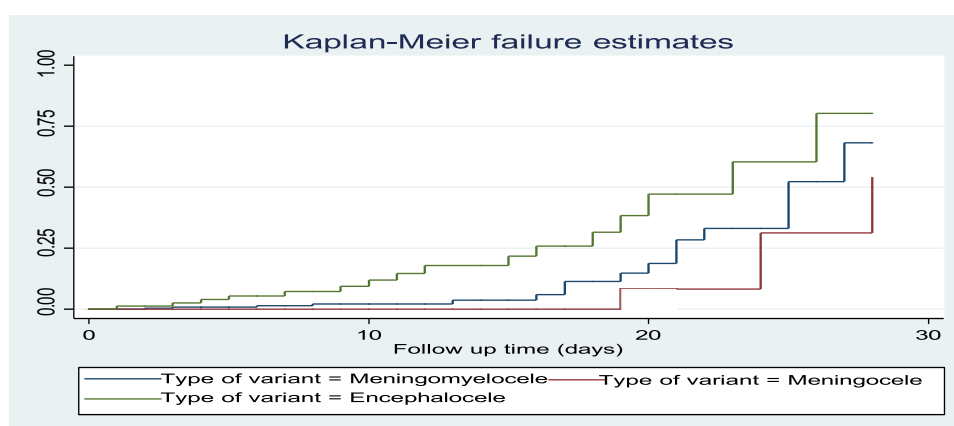


Figure 5 The Kaplan-Meier failure estimates of time to death, with categories of type of variant among neonates with neural tube defects in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410).

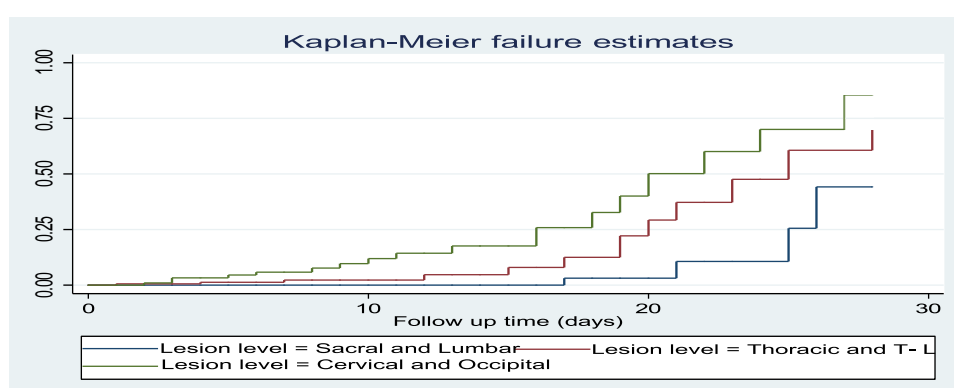


Figure 6 The Kaplan-Meier failure estimates of time to death, with categories of lesion level among neonates with neural tube defects admitted to Z.M.H and St. P.S.H., Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410).

Time to Death Predictors for Newborns with Neural Tube Problems

Cox regression analysis, both bivariate and multivariate, was used to determine time to death predictors for infants with neural tube defects. Birth weight, gestational age, lesion level, type of variation, hydrocephalus, Chiari-II malformation, sepsis, and motor function deficit were therefore linked to time to death at a P-value of less than 0.25, according to the results of the bivariate analysis. Only birth weight, gestational age, variant type, lesion level, hydrocephalus, and Chiari-II malformation showed a statistically significant correlation with time to death in neonates with neural tube defects in the multivariable analysis (P-value < 0.05).

As a result, preterm newborns had a 2.62-fold increased risk of dying before their due date (AHR: 2.62, 95% CI 1.12, 6.14). Likewise, neonates with low birth weight had a 2.62-fold increased risk of death in comparison to those with normal birth weight (AHR: 2.62, 95% CI 1.13, 6.10). Additionally, the results indicated that newborns with neural tube abnormalities that had encephalocele had a 3.77-fold increased risk of death compared to those who had meningocele (AHR: 3.77, 95% CI 1.65, 8.62).

The hazard of death for neonates who had neural tube defects at the cervical and occipital level was 3.97 times higher than their counterparts with sacral and lumbar level lesion (AHR: 3.97, 95% CI, 1.17, 13.49). Besides, the risk of death among neonates with neural tube defects who had hydrocephalus was 3.98 times higher than to those who had not (AHR: 3.98, 95% CI 1.55, 10.21). Likewise, neonates with neural tube defects who had Chiari-II malformation had 2.40 times increased hazard of time to death compared to neonates without Chiari-II malformation (AHR: 2.40, 95% CI 1.03, 5.57) (Table 4).

Table 4 Result of the Bivariate and Multi Variate Cox Regression Analysis of Time to Death of Neonates with Neural Tube Defects Admitted in Addis Ababa, Ethiopia; from Jan. 2018–Dec. 2022 (n = 410)

Variables	Category	Status		CHR (95% CI)	AHR (95% CI)	P-value
		Died n (%)	Censored n(%)			
Gestational age	28-36 Week	20(24.4)	62(75.6)	4.83(2.46–9.48)	2.62(1.12–6.14)*	0.010
	37-42 Week	15(4.6)	313(95.4)	I	I	
Birth weight	1500-2499	26(24.8)	79(75.2)	6.32(2.95–13.54)	2.62(1.13–6.10)*	0.014
	≥2500	9(3.0)	296(97.0)	I	I	
Type of NTD	Encephalocele	16(20.5)	62(79.5)	2.83(1.41–5.67)	3.77(1.65–8.62)*	0.002
	Meningocele	3(3.3)	87(96.7)	0.43(0.13–1.50)	0.83(0.22–3.21)	
	Meningomyelocele	16(6.6)	226(93.4)	I	I	
Lesion level	Cervical and Occipital	18(19.1)	76(80.9)	9.28(3.13–27.48)	3.97(1.17–13.49)*	0.042
	Thoracic and Thoraco-lumbar	13(8.5)	140(91.5)	4.12(1.34–12.68)	3.09(0.87–10.99)	
	Sacral and Lumbar	4(2.5)	159(97.5)	I	I	
Motor function deficit	Yes	28(11.7)	211(88.3)	2.63(1.14–6.02)	1.32(0.49–3.48)	0.502
	No	7(4.1)	164(95.9)	I	I	
Hydrocephalus	Yes	22(11.2)	174(88.8)	3.19(1.55–6.57)	3.98(1.55–10.21)*	0.005
	No	13(6.1)	201(93.9)	I	I	
Chiari-II malformation	Yes	21(16.3)	108(83.7)	3.12(1.58–6.16)	2.40(1.03–5.57)*	0.022
	No	14(5.0)	267(95.0)	I	I	
Sepsis	Yes	21(20)	84(80)	2.66(1.34–5.28)	0.72(0.29–1.75)	0.825
	No	14(4.6)	291(95.4)	I	I	

Note: *Statistically significant at P-value of <0.05.

Discussions

This study was conducted to assess the time to death and identify the predictors in neonates with NTDs in Addis Ababa, Ethiopia. At the end of the follow-up, 35 patients were died, and 375 patients were censored. That resulted in a cumulative incidence of deaths of 8.54% over 5 years. This finding is consistent with studies conducted in Turkey, 7.5%,²⁴ Bahir-dar, 7.3%,²⁵ and Zambia, 7%.²⁶ But it is significantly lower than previous studies conducted in Addis Ababa, 41%,¹¹ Uganda, 34%²⁷ and Democratic Republic of Congo, 15%.²⁸ This disparity might be explained by the possible improvements in neonatal medical and neurosurgical care, and accessibility of skilled health care providers by the community over the past five years.

On the other hand, our finding was higher than prior studies done in the multiple state of United States 4.4%²⁹ and a study done in the state of Texas 3.1%.³⁰ It may be because of neonates and fetuses with neural tube defects receive cutting-edge medical and neurosurgical treatment in developed nations.

Preterm neonates with neural tube defects had a higher hazard of death compared to term neonates. This result is incongruent with studies conducted in United Kingdom, New York and Finland.^{23,31,32} The reason could be preterm babies, encounter nutritional problems, difficulty in thermoregulation and maintaining glucose balance. These problems could be responsible for the increased hazard of time to death, due to their propensity to prolong pre- or post-neurosurgical recovery time and length of hospitalization.

The immune system and other bodily defense mechanisms are suppressed in preterm infants, which predispose them to infections by pathogenic microorganisms. Additionally, due to their immature lung, preterm neonates are more likely to experience respiratory distress syndrome than term newborn.³³ This further complicates the clinical course of the defect, thereby negatively affecting the prognosis and fastening the time to death.

Low birth weight neonates with neural tube defects had a higher hazard of death compared to normal birth weight neonates, which is consistent with a study conducted in California, Texas, Finland and Ghana.^{14,30,32,34} The reason might be that, LBW neonates with NTDs are more likely to be preterm and, as a result, they are more prone to experience preterm-related problems that could shorten their survival duration. Thus, prevention of preterm birth and improving the care provided to this population groups is paramount in lowering the risk.

Neonates who had cervical and occipital level lesion had nearly threefold higher hazard of death than those with Sacral and Lumbar level lesion. This is in line with studies done in United States,³⁵ United Kingdom²³ and Uganda.¹⁵ This may be because of higher level lesions are associated with severe malformation of the brain and non-brain associated anomalies. Thus indicates, the higher the lesion, the poorer the outcome. Newborns with encephalocele were found to have higher hazard of time to death than neonates with meningomyelocele. This finding was in accordance with the study conducted, in Turkey.³⁶ This possibly explained by its association with postoperative recurrent apnea, delay in surgical repair, hydrocephalus and other CNS and extra CNS anomalies. Also, positioning and access difficulties with mask ventilation and intubation of patients with encephalocele may increase the risk of early mortality.

In this study, hydrocephalus was a positive predictor of time to death among neonates diagnosed with NTDs, this is consistent with studies conducted in, Germany, United Kingdom, and Ireland.^{37–39} This may be explained by its association with, Chiari II malformation, and frequent ventriculoperitoneal shunt failure that need reinsertion, which render patients to have CSF infection and resultant complications thereby increasing the hazard of time to death.

Moreover, this study revealed that neonates with Chiari II malformation had higher hazard of death compared to their counterpart. This is consistent with a study conducted in Brazil and Florida, United States.^{40,41} The possible reason for this could be the associated respiratory dysfunction and failure that happens as a result of brainstem compression. Swallowing problems in those neonates may also negatively affect their nutritional status making them more susceptible to other complications, which reduces their survival time.

Most of the findings from this study were comparable from a study conducted in British Columbia between 1971 and 2016, the number of new instances of myelomeningocele (MMC) decreased, but survival rates increased. Long-term results, however, have not improved much in spite of earlier and more extensive postnatal restoration.⁴² When compared to postnatal correction, prenatal MMC repair has been linked to long-lasting improvements in posterior fossa imaging of Chiari II malformation at school age. In order to sustain optimal function, enhance life satisfaction, and promote long-term survival, people with MMC need ongoing, multidisciplinary, lifelong follow-up and therapy. To maximize healthcare delivery, follow-up and rehabilitation must be approached methodically.^{43,44}

Strength and Limitation of the Study

This study has several notable strengths, including a relatively large sample size and the application of advanced survival analysis techniques, which enhance the reliability and precision of the findings. The findings can guide resource allocation, clinical decision-making, and training for healthcare providers in neonatal intensive care units, ultimately contributing to reduced neonatal mortality. The results also highlight the need for future research to explore the effectiveness of specific interventions; such as early surgical treatment, improved nutritional support, and enhanced postnatal monitoring in improving survival outcomes for neonates with NTDs in both urban and rural settings.

The study is limited by its retrospective nature. Thus, the limited information that could be gleaned from the patients' medical record may have restricted the identification of other predictors of time to death. Furthermore, selection bias may have been introduced due to the exclusion of incomplete or missed medical charts.

Conclusion

This study confirms that NTDs remain a significant cause of neonatal mortality in Addis Ababa. Key predictors of mortality include prematurity, low birth weight, cervical and occipital lesion levels, hydrocephalus, encephalocele, and Chiari II malformation. Reducing mortality requires a multipronged approach involving enhanced prenatal screening, routine folic acid supplementation, prompt referral to specialized care, and improved neonatal and neurosurgical management. Establishing a national surveillance system for congenital anomalies and associated outcomes could support data-driven policy and improve child survival in Ethiopia.

Ethical Considerations

After the proposal approval, ethical clearance was obtained from the Institutional Review Board (IRB) of the Department of Nursing at Addis Ababa University (Ref/09/SNM/15). A support letter and ethical clearance were submitted to St. Peter's Specialized Hospital and the Addis Ababa Public Health Research and Emergency Management Directorate at Zewditu Memorial Hospital. As the study relied on patient medical records, informed consent was waived by the study hospitals in accordance with the Declaration of Helsinki. Access to registration books and medical records was granted before data collection. To maintain confidentiality, data were coded, password-protected during entry and analysis, and no participant names were recorded.

Abbreviations

ETOPFA, Elective Termination of Pregnancy for Fetal Anomaly; MMC, Myelomeningocele; MSAFP, Maternal Serum Alpha-Fetoprotein; NTD, Neural Tube Defects; SBD, Spina Bifida; SPH, Saint Peter Hospital; ZMH, Zewditu Memorial Hospital.

Data Sharing Statement

All data and information used in this study are available from the corresponding author upon request.

Acknowledgments

We are very grateful to the Department of Nursing College of Health Sciences, Addis Ababa University (AAU), and Dilla University (DU) for supporting the study. The content is the sole responsibility of the authors and does not represent the official views of the AAU, DU or others. We would also like to thank the NICU staff of the Z.M.H. and St. P.S.H., the study participants, the data collectors and to those all who assisted us during the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is 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.

Funding

The study's authors attest that financing was obtained from Addis Ababa University.

Disclosure

Regarding this work, the authors disclose no conflicts of interest.

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