Incidence and predictors of mortality among low birth weight neonates in the first week of life admitted to the neonatal intensive care unit in Northwestern Ethiopia comprehensive specialized hospitals, 2022. Multi-center institution-based retrospective follow-up study

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Abstract

Background Globally, a high number of neonatal mortalities occurs in the first week of life, particularly among low birth weight neonates in low-income countries, including Ethiopia. However, there is limited evidence on the early neonatal mortality of low-birth-weight neonates in Ethiopia. Therefore, this study aimed to assess incidence and predictors of mortality among low-birth-weight neonates in their first week of life admitted to the neonatal intensive care unit in Northwestern Ethiopia Comprehensive Specialized Hospitals, 2022.

Methods A multi-center retrospective follow-up study was conducted from March 21, 2020 to March 1, 2022, among 761 early neonates with low birth weight admitted in Northwestern Ethiopia Comprehensive Specialized Hospitals. The study participants were selected using simple random sampling technique. Data were collected using a data abstraction checklist ,and checked for completeness and entered into EPI data version 4.6, then exported to STATA 14 for analysis. Kaplan Meier failure curve and log-rank test were used to estimate and compare the probability of death. Both bivariable and multivariable Weibull regression models were fitted to identify predictors of mortality. Finally, a hazard ratio with 95% CI was computed, and variables having a p-value < 0.05 were considered as a significant predictor of mortality.

Results The incidence of mortality among low birth weight neonates in their first week of life was 75.63 per 1000 neonate day observation (95% CI: 66.76–85.67), preeclampsia (AHR = 1.77;95% CI:1.32-2.36s), perinatal asphyxia (AHR = 1.64; 95% CI:1.14–2.36), respiratory distress syndrome (AHR = 1.76 95% CI:1.31–2.34), necrotizing

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enterocolitis (AHR = 2.78 95% CI;1.79–4.32), prematurity (AHR = 1.86; 95% CI:1.30–2.67), and birth weight < 1000gram (AHR = 3.13;95% CI: 1.91–5.12) and 1000–1499 gram (AHR = 1.99; 95% CI:1.47–2.68) were predictors.

Conclusion The incidence of early neonatal mortality in low birth weight neonates was incredibly higher than the overall early neonatal mortality in Northwest Ethiopia (Amhara region). Preeclampsia, perinatal asphyxia, respiratory distress syndrome, necrotizing enterocolitis, prematurity, and birth weight were predictors of mortality. Therefore, stakeholders shall give early identification and emphasis on preventable and treatable predictors. Furthermore, the health care provider shall give education about the importance of breastfeeding, and Antenatal and postnatal care.

Keywords First week of life, Incidence, Mortality, Low birth weight, Predictors

Background

Globally, three-fourths of neonatal mortality occurs in the first week of life [1]. A high number of Early Neonatal Mortality (ENM) occurs among Low Birth weight (LBW) neonates [2]. These neonates are 20 times more likely to die than normal birth-weight neonates [3, 4]. Early Mortality among LBW neonates is continued to be a major public health problem, particularly in middle-income, and low-income countries [5]. According to World Health Organization (WHO) report, in 2020, above 2.4 million neonates died annually, and 80% of them are LBW [5, 6]. The first week of life is a critical period for the survival of LBW neonates. Of the total neonatal deaths, 75% occurs during the first weeks of life, with one-third of deaths occurring on the first day of birth [1, 6]. Specifically in Southeast Asia, the mortality of LBW neonates ranges from 19 to 31% [7], and in Sub-Saharan Africa, the mortality of these neonates ranges from 21% in females to 23.9% in males [8].

The incidence of ENM among LBW varies across the country with the highest incidence of ENM occurring in low-income countries, for instance in Bangladesh it was 112 per 1,000 neonate day observations, in Brazil 52 per 1,000 neonates [9], in India 21.22 per 1000 live births [10], Burkina Faso 1.93 per 1000 neonate/day [11], and in Bahir Dar, Ethiopia 22.16 per 1000 neonate day observation [12].

Ethiopia aimed to reduce the Neonatal Mortality Rate (NMR) from 29 to 1000 live births in 2016 [13] to 11 per 1000 live births in 2019/2020, including LBW neonates [14]. Despite the government's aim of reducing Neonatal Mortality (NM), paradoxically it had been increased to 33/1000 live births in 2019, from this, the mortality of LBW neonates is a major public health problem [15]. In Ethiopia, the mortality of LBW neonates ranges from 11.0 to 37.8% [12, 16–18]. Overall, early neonatal mortality in the Amhara region is 43 per 1000 live births, which is the highest figure in the country [13].

These studies suggested that the predictors of mortality among LBW neonates are maternal age [12], Antenatal care(ANC) follow-up [16], neonatal age, residence, sex, type of pregnancy [19, 20], birth weight [9, 19, 21], sepsis [12, 18, 22], perinatal asphyxia [21, 23, 24], Respiratory Distress Syndrome(RDS) [12, 18, 25, 26], prematurity [12, 16, 25, 27–29], Necrotizing Enter Colitis(NEC) [12, 26, 30, 31], 1st, and 5th minute (Appearance, Pulse, Grimace, Activity, Respiration) (APGAR) score [19, 32], place of delivery, preeclampsia [33, 34], maternal diabetes mellitus (DM) [17, 25], and maternal Human Immunodeficiency Virus(HIV) infection [13, 35]. Nevertheless, the incidence and predictors of mortality among LBW neonate, specifically in their first week of life is not fully addressed.

To tackle this problem, and increase the survival of LBW neonates, efforts have been made globally as well as nationally. For instance, WHO is working with the Ministry of Health (MoH) and other partners to expand the quality of services for LBW babies [36]. Interventions like the provision of adequate nutrition for adolescent girls were done to reduce mortality among LBW neonates [37]. In addition, the Sustainable Development Goal (SDG 3) focuses on reducing neonatal mortality to below 12 per 1000 live births by 2030 [38]. Furthermore, Ethiopia accepted initiatives to decrease the mortality of LBW neonates [39], and currently, planned to reduce neonatal mortality from 33 to 1000 live births to 21 per live births by the year 2024/2025 [40].

Despite these efforts and strategies, neonatal mortality remains high [35], and increased from 29 to 33 per 1000 live birth since 2016 [13, 35], Despite this problem, the previous studies conducted in Ethiopia have not focused on the critical period of life before 7 days among LBW neonates, and, there is limited evidence on this subgroup of neonates in the critical period of life regarding the incidence of ENM and its predictors among LBW neonates in the study setting. Therefore, estimating the incidence, and identifying predictors among high-risk groups in the critical period of life are the cornerstones to improve LBW neonate survival, progress toward the national plan, designing appropriate interventions, and providing valuable clinical information for health professionals. Hence, this study aimed to assess the incidence and predictors of mortality among LBW neonates in the first week of life admitted to Comprehensive Specialized Hospitals of Northwest Ethiopiain.

Methods

Study setting, design, and period

An institution-based multi-center retrospective follow-up study was conducted using data of LBW neonates from March 21, 2020 to March 1, 2022 (the data were extracted from May 1 to June 26, 2022) in Neonatal Intensive Care Unit (NICU) of Northwest Ethiopia (West Amhara) Comprehensive specialized hospitals. Comprehensive Specialized Hospitals in the Northwest part of Ethiopia (West Amhara region) are the University of Gondar (UoG), Felege hiwot, Tibebe Ghion, Debre Tabor, and Debre Markos. UoGCSH is found in Gondar town, and this hospital has an average annual admission of 726 LBW neonates and 528 of them were admitted in the first week. Felege hiwot and Tibebe Ghion CSH are found in Bahir Dar city. Felege Hiwot CSH has average annual admission of 720 LBW neonates and 504 of them were admitted in the first week. Tibebe Ghion has an average annual admission of 690 LBW neonates, and 484 of them were admitted within the first week. Debre Tabor CSH is found in Debre Tabor town. This hospital has an average annual neonatal admission of 512 LBW neonates, and, 408 of them were admitted in the first week. Debre Markos CSH is found in Debre Markos town, and this hospital has an average annual admission of 612 LBW neonates and 444 of them were LBW early neonates. These Hospitals have NICU with mixed health professionals (neonatal and comprehensive nurses, general practitioners, pediatricians, and other staffs). The major services in the NICU include general neonatal care services, blood and exchange transfusion, phototherapy, and ventilation support such as Continuous Positive Air Pressure (CPAP).

Study population

All LBW neonates in the first week of life admitted to the NICU of Northwest Ethiopia Comprehensive Specialized Hospitals were considered as the source population, and all low birth weight neonates in the first week of life admitted to the NICU of Northwest Ethiopia Comprehensive Specialized Hospitals from March 21, 2020 to March 1, 2022 were taken as a study population.

Eligibility criteria

LBW neonates in their first week of life who were admitted to NICU from March 21, 2020, to March 1, 2022, were included, Whereas, Neonates with an incomplete chart (outcome status and charts with one of the following predictor is missed (gestational age, birth weight, neonatal age, sex, type of pregnancy, place of delivery, date of admission, and discharge)) were excluded.

Sample size estimation and sampling technique

The sample size was determined using STATA 14, using the Cox proportional hazard model by considering the following assumptions: confidence level (95%), Power (80%), a 28.35% Probability of an event, and 1.483 hazard ratio of the predictor (maternal age above 35) [12], 5% Margin of error, and 10% probability of withdrawal (chart attrition). Accordingly, the final estimated sample size was 793 LBW neonates chart. Within two years, the hospitals had a total of 4752 LBW early neonate admissions. Accordingly, the total sample size was proportionally allocated to each hospital, and the neonate's chart was selected by a simple random sampling technique using a computer-generated random number in Excel.

Variables of the study

The dependent variable of the study was mortality in the first week of life, whereas the independent variables include (1) socio-demographic variables such as (maternal age, sex of the neonate, age of the neonate, place of delivery, residence). (2) Maternal medical factors such as maternal DM, HTN, HIV/AIDS, TB, Anemia, and other illnesses (STI, UTI). (3) Maternal obstetric factors such as (type of pregnancy, gravidity, parity, PROM, APH, mode of delivery, preeclampsia, ANC follow-up, corticosteroid administration), and (4) Neonate's clinical related variables such as (PNA, RDS, sepsis, jaundice, hypothermia, hypoglycemia, NEC, 1st & 5th minute APGAR score, breastfeeding, congenital anomalies, IUGR, birth weight, gestational age).

Operational definition

Low birth weight Weight at birth less than 2,500 g regardless of gestational age [3].

Early neonatal mortality The death of the newborn from the time of birth up to seven completed days of life [2, 41].

Event Death of LBW neonates at a specific time (day) within seven days of age.

Censored LBW neonates who left the follow-up (survived over the follow-up period, lost to the follow-up, transferred/ referred to other health facilities, and left against medical treatment).

Extremely low birth weight Neonates born with less than 1000 gm of birth weight [6].

Follow-up time The time from admission to NICU to either death or censorship occurs.

Prematurity Neonate born before 37 completed weeks of gestational age [42].

Survival status Outcome of neonates, either death or censored.

Very low birth weight Neonates born with (1000–1499 gm) of birth weight [42].

Data abstraction checklist and procedures

The data abstraction checklist was adapted by reviewing different relevant literature, and guidelines [8, 12, 17, 19, 21, 42–44]. It contains four parts: socio-demographic characteristics of mothers and neonates, maternal medical disorders, obstetric, and gynecological factors, neonate's clinical-related variables of LBW neonates, and outcome measures. The data were retrospectively collected by 5 experienced BSc nurses and supervised by 4 experienced BSc nurses. The medical registration number of LBW neonates who were admitted in the early neonatal period from March 21, 2020 to March 1, 2022 was first obtained from the FMOH registration book. Then, the required number of neonates' medical charts was selected by a simple random sampling technique according to eligibility criteria.

Data quality control

The data abstraction checklist was evaluated by the expert researcher, and then a pretest was done on 5% of the sample size in a similar setting, and necessary

Table 1 Socio-demographic characteristics of the neonates and mothers admitted to NICU of Northwest Ethiopia CSH from March 2020 to March 2022 (N = 761)

Variable	Number	Percent	Status	
			Death	Censored
Age of the neonate in days				
≤1 day	525	68.99	186	339
2–3 days	143	18.79	45	98
4–7 days	93	12.22	16	77
Sex				
Male	395	51.91	118	277
Female	366	48.09	129	237
Maternal age				
≤20	105	13.57	39	66
21–34	537	70.37	180	357
≥35	119	15.64	28	91
Residence				
Urban	445	58.48	142	303
Rural	316	41.52	105	211
Place of delivery				
Health institution	731	96.06	242	489
Out-of-health institution	30	3.94	5	25

amendments were done. One-day training was given to data collectors and supervisors focusing on the purpose of the study, the data collection tool, data collection methods, and ethical concerns during the data collection period. All the collected data were checked for their completeness and consistency by the data collectors and supervisors daily.

Data processing and analysis

The data were cleaned, coded, and entered into Epi-Data version 4.6.0.6, and the analysis was done using STATA version 14 statistical software. The outcome was dichotomized into death, coded as "1", and censored coded as "0". The variance inflation factor was used to assess multi-collinearity. The incidence rate of mortality was calculated for the entire follow-up by dividing the number of new cases of mortality of LBW early neonates by the total person-days of follow-up. Kaplan Meier failure curve was used to estimate the time to death during the follow-up. The log-rank test was employed to compare statistical differences between groups of independent variables. The Schoenfeld residual global test for proportionality assumption was checked, and its (P-value = 0.4282) was used as a suggestive of satisfying the assumption. The log-likelihood and Akaike Information Criteria (AIC) were applied to select the best-fitted model, and a model with minimum AIC was considered a fitted model. Based on this the Weibull regression model with the (AIC = 1196.251) value was the fitted model. The goodness of fit of the model was also checked using the Cox-Snell residual test, and it was close to the bisector. Variables with P-value < 0.25 in the bi-variable analysis were entered into the multivariable Weibull regression model analysis. Crude and adjusted hazard ratios with 95% CI, were used to determine the strength of the association. In multivariable analysis variables having a p-value < 0.05 were considered as predictors of mortality.

Results

Socio-demographic characteristics of mother-neonates pair

A total of 793 LBW neonates' medical charts were reviewed with a completeness rate of 761(95.96%) charts. Of the total included neonates, about half of the participants 395 (51.91%) were male. Above two-thirds, 525 (68.99%) of neonates were admitted within 24 h of birth. Most 537(70.37%) of the mothers were in the age category of 21–34 years old. The median age of the mothers was 28 (IQR 23, 31). (Table 1).

Maternal obstetric and gynecological-related characteristics

Of the total enrolled mothers in this study, the Majority 696 (91.46%) had ANC follow-ups in nearby health

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institutions. Nearly three fourth of neonates were delivered via spontaneous vaginal delivery (SVD), and 567(74.51%) were singleton pregnancies. About one-fourth of mothers 203 (26.68%) had preeclampsia, and 185 (24.31%) mothers were taking corticosteroid treatment(Table 2).

Maternal medical-related characteristics of study participants

Among the total enrolled mothers in this study, 19(2.5%) had chronic hypertension, 39 (5.12%) had HIV/AIDS, and 17(2.23%) had other comorbidities ((Urinary Tract infection (UTI), syphilis, and Hepatitis B Virus (HBV)) (Table 3).

Clinical related and other characteristics of LBW early neonates

Above two-thirds 512(67.28%) of low birth weightearly neonates were premature, and the median gestational age was 35 weeks with an interquartile quartile range

Table 2 Maternal obstetric and gynecological related characteristics of low birth weight early neonates in Northwest Ethiopia CSH from March 21, 2020 to March 1, 2022 (N = 761)

Variables	Frequency%	Status	
		Death (%)	Censored (%)
ANC			
Yes	696(91.46)	223(90.28)	473(92.02)
No	65 (8.54)	24(9.72)	41(7.98)
Type of pregnancy			
Single	567(74.51)	167(67.61)	400(77.82)
Multiple	194(25.49)	80(32.39)	1114(22.18)
Mode of delivery			
SVD	565(74.24)	182(73.68)	383(74.51)
Instrumental	29(3.81)	5(2.02)	24 (4.67)
CS	167(21.94)	60(24.29)	107(20.82)
Gravidity			
Primi-gravida	147(19.32)	40(16.19)	107(20.82)
Multi-gravida	614(80.68)	207(83.81)	407(79.18)
Parity			
Primi-para	415 (54.53)	127(51.42)	288(56.03)
Multipara	346 (45.47)	120(48.58)	226(43.97)
Corticosteroid Treatment	185(24.31)	71(28.74)	114(22.18)
Yes	576(75.69)	176(71.26)	400(77.82)
No			
Preeclampsia			
Yes	203(26.68)	105(42.51)	98(19.07)
No	558(73.32)	142(57.49)	416(80.93)
PROM			
Yes	124 (16.29)	46(18.62)	78((15.18)
No	637(83.71)	201(81.38)	446(84.82)
APH			
Yes	71(9.33)	29(11.74)	42(8.17)
No	690(90.67)	218(88.26)	472(91.83)

ANC: Antenatal care, PROM: Premature rupture of membrane, APH: Antepartum hemorrhage, SVD = Spontaneous vaginal delivery, CS = Cesarean section

of 5 weeks. Three-fourths of neonates 570(74.90%) weighed between 1500, and 2499 g with a median weight of 1750±600 IQ. The common medical problem among LBW early neonates was sepsis (65.83%), and RDS was the leading cause of death in 167(62.75%). Other common medical problems include jaundice, PNA, NEC, IUGR, hypoglycemia, and congenital anomalies (Table 4).

Incidence of mortality in the first week of life and overall survival outcome of the follow-up among LBW neonates

In this study, a total of 761 LBW early neonates were followed for up to 7 days of age starting from the date of admission. Among those Low birth weight neonates in the first week of life, 247(32.46%) died, 170 (22.34%) were discharged with improvement, 5(0.66%) transferred to other health institutions, 6(0.79%) lost follow-up, 15(1.97%) left against medical advice and 318 (41.79%) were surviving beyond the follow-up period. Most 80 (32.3%) of neonates died within the first day after admission, 47(19.03%) on the second day, 46 (18.2%) on the third day, 27(10.93%) on the fourth day, 27(10.93%) in the fifth day, 13(5.26%) in the sixth day, and 7(2.83%) were died in the seventh day after admission. The total neonate-day observation during the entire follow-up time was 3266 person-days.

In this study, the overall incidence of early neonatal mortality was 75.63 per 1000 neonate day observations (95% CI: 66.76–85.67). The incidence of mortality at the end of the first day was 105.12 (95% CI; 84.44 -130.88), on the second day 73 0.09 (95%CI: 54.91–97.28), on the third day 84.24(95% CI: 63.10-124.47) on the fourth day 61.22 (95% CI: 41.98–89.27), on the fifth day 74.58 (95% CI: 51.14–108.7), on the sixth day 44.52(95% CI:25.85–76.67), and on the seventh day 31.16(95%CI: 15.10-66.44) per 1000 neonate. Similarly, the incidence rate of mortality among ELBW was 223.30 (95% CI; 148.38-336.03), among VLBW, it was 156.70 (95% CI; 128.43–191.20), and among LBW (1500-2499gm) neonates, 49.92 (95% CI; 41.95–59.40) was observed per 1000 neonate days' observation period.

Overall failure function

*The mean time to mortality of the entire cohort was 5.48 (95% CI: 5.32–5.65) days. The cumulative probability of death at the end of the 1st day was 0.108 (0.088–0.133), at the end of the 3rd day, it was 0.25 (0.22–0.28), and at the end of the 7th day, it was 0.423(0.38, 0.47).In this study, as hospital stay increases, the hazard of death increases, and the survival probability was decreased (*Fig. 1*).*

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Table 3 Maternal medical characteristics of low birth weight early neonates admitted to NICU of Northwest Ethiopia Comprehensive Specialized Hospitals from March 21, 2020 to 1 March, 2021(N = 761)

Variable	Frequency (%)	Status	
		Death %	Censored %
Chronic hypertension			
Yes	19 (2.50)	8(3.24)	11(2.14)
No	742(97.50)	239(96.76)	503(97.86)
Maternal DM			
Yes	11(1.45)	5(2.02)	6(1.17)
No	750(98.55)	242(97.98)	508(98.83)
Maternal HIV			
Yes	39(5.12)	21(53.85)	18(46.15)
No	722(94.88)	226(31.30)	496(68.70)
TB			
Yes	13(1.71)	6(2.43)	7(1.36)
No	748(98.29)	241(97..57)	507(98.64)
Anemia			
Yes	13(1.71)	5(2.02)	8(1.56)
No	748 (98.29)	242 (97.98)	506(98.44)
Other comorbidities			
Yes	17(2.23)	6(2.43)	11(2.14)
No	744(97.77)	241(95.57)	503(97.86)

DM: Diabetes mellitus, TB: Tuberculosis, HIV: Human immune deficiency virus

Comparison of failure function for different categorical variables

In this study, neonates born from a mother with pre-eclampsia had a higher risk of death than neonates born from a mother without preeclampsia. The mean hazard time to death was 4.71 days (Fig. 2A). Similarly, LBW early neonates with PNA had an increased risk of death than LBW neonates who did not have PNA, and the mean time of death was 4.69 days (95% CI 4.17–5.21) as compared with their counterparts (Fig. 2B).

The result of this study also showed that LBW neonates with RDS had lower survival than their counterparts. The mean hazard time to mortality was 5 days (95% CI 4.75–5.25) as compared to neonates without RDS (5.9 days) (Fig. 2c). Similarly, LBW neonates with NEC had a higher risk of death as compared with their counterparts. The mean time to death was 4.42 days (95% CI: 3.71–5.13) as compared to LBW neonates without NEC (5.55 days) (Fig. 2D).

In this study, neonates having ELBW (<1000gm) and VLBW (1000-1499gm) had lower survival time than low birth weight neonates (1500-2499gm). In the present study, nearly all 23 (69.70%) ELBW neonates, and 97 (61.39%) VLBW neonates died. The mean hazard time to death for EVLBW and VLBW was 3.48 days, and 4.38 days respectively, as compared to those LBW neonates with a mean hazard time to death of 5.95 days (Supplementary file 1). In addition, Premature LBW neonates were at high risk of death as compared to those term

Table 4 Clinical characteristics of low birth weight early neonates admitted to Northwest Ethiopia CSH from March 21, 2020 to March 1, 2022. (N = 761)

Variable	Frequency %	Status	
		Died %	Censored%
Birth weight in gram			
≤ 999	33(4.34)	23(9.31)	10(1.95)
1000–1499	158(22.86)	97(39.27)	61(11.87)
1500–2499	570(74.90)	127(51.42)	443(86.19)
Gestational Age in week			
<37	512(67.28)	203(82.19)	309(60.12)
≥37	249(32.72)	44(17.81)	205(39.88)
First-minute APGAR score			
<7	272(35.74)	123(49.80)	149(28.99)
≥7	489(64.26)	124(50.20)	365(71.0)
Fifth-minute APGAR score			
<7	71(9.33)	47(19.03)	24(4.67)
≥7	690(90.67)	200(80.97)	490 (95.33)
Breastfeeding			
Yes	712(93.56)	228(92.31)	484 (94.16)
No	49(6.44)	19(7.69)	30 (5.84)
PNA			
Yes	87(11.43)	47(19.03)	40(7.78)
No	674(88.57)	200(82.19)	474(92.22)
Sepsis			
Yes	501(65.83)	162(67.61)	339(65.95)
No	260(34.17)	85(32.39)	175(34.05)
RDS			
Yes	356(46.78)	167(62.75)	189(36.77)
No	405(53.22)	80(37.25)	325(63.23)
Jaundice			
Yes	104(13.67)	22(8.91)	82(15.95)
No	657(86.33)	225(91.09)	432(84.05)
NEC			
Yes	46(6.04)	26(10.53)	20(3.89)
No	715(93.96)	221(89.47)	494(96.11)
IUGR			
Yes	41(5.39)	19(7.69)	22(4.28)
No	720(94.61)	228(92.31)	492(95.72)
Congenital anomalies			
Yes	29(3.81)	7(2.83)	22(4.28)
No	732(96.19)	240(97.17)	492(95.72)
Hypothermia			
Yes	269(35.35)	101(40.89)	168(32.68)
No	492(64.65)	146(59.11)	346(67.32)
Hypoglycemia	29(3.81)	12(4.86)	17(3.31)
Yes			
No	732(96.19)	235(95.14)	497(96.69)

PNA = perinatal Asphyxia, APGAR = Appearance, Pulse, Grimace, Activity, Respiration, NEC = Necrotizing enterocolitis, RDS = respiratory distress syndrome, IUGR = Intrauterine growth restriction
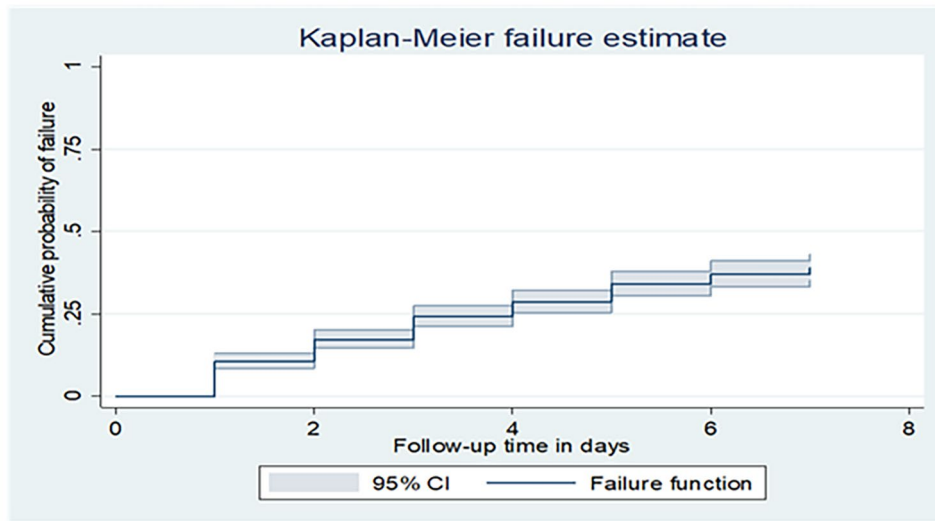
Fig. 1 The overall Kaplan Meier failure estimate of mortality among low birth weight in the first week of life in Northwest Ethiopia Comprehensive Specialized Hospitals, from March 21, 2020, to March 1, 2022
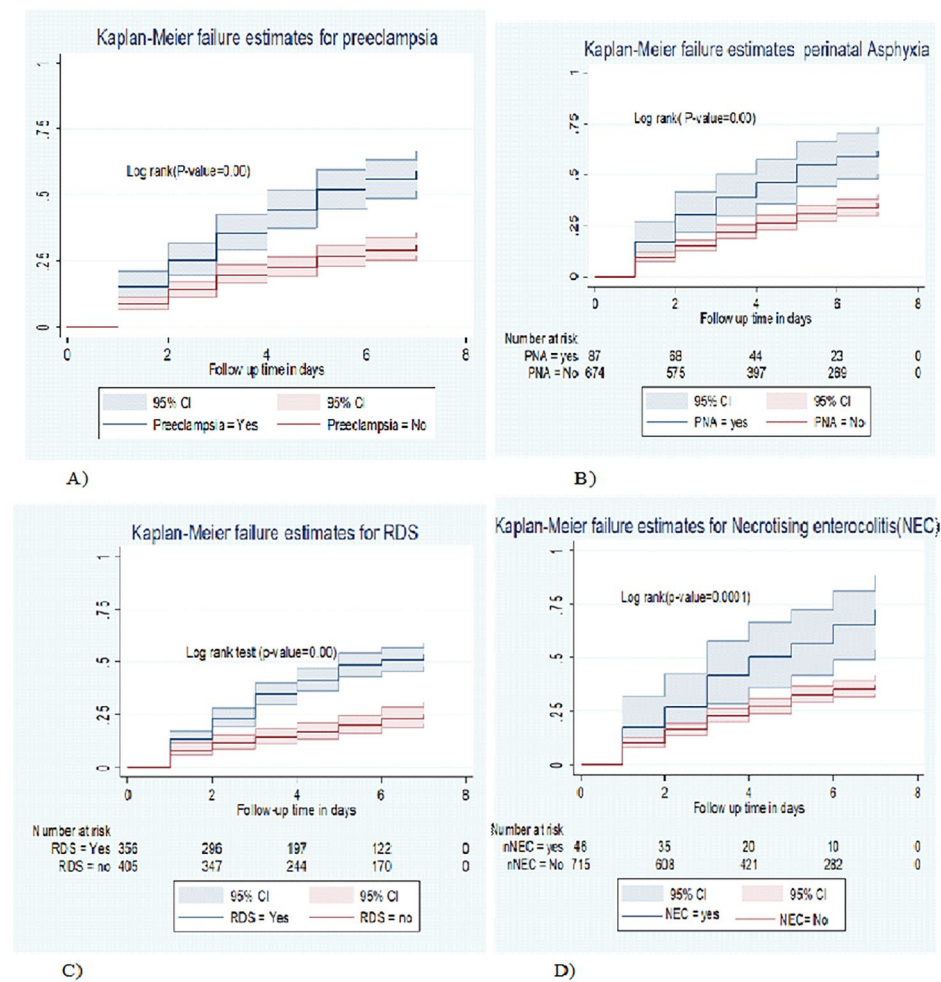

Fig. 2 The Kaplan Meier failure estimates of low birth weight early neonates, by (A) Preeclampsia, (B): PNA, (C): RDS, (D); NEC in Northwest Ethiopia CSH, from March 21, 2020, to March 1, 2022

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LBW neonates (Supplementary file 1). These differences were statistically significant with a (P-value ≤ 0.0001) in the log-rank test.

Proportional hazard assumption test by schoenfeld residuals

The Cox proportional hazard assumption was checked using the Schoenfeld residuals test individually and simultaneously (globally). The test showed that the P-value for each covariate and the whole covariates simultaneously were above 0.05 (P-value = 0.4282).

Model comparison and diagnostics

Model comparison of both the semi-parametric and parametric hazard models were done statistically using information criteria (AIC, BIC) to select the most parsimonious model for the data set. Based on this, the Weibull regression model with the **(AIC = 1196.251)** was the parsimonious model (Table 5).

The goodness of fit for the fitted model was also checked using the Cox-Snell residual test and as shown in the figure Weibull regression model was adequate (Fig. 3).

Predictors of mortality

In the bi-variable Weibull regression sex, mode of delivery, preeclampsia, APH, antenatal corticosteroid treatment, gravidity, maternal HIV/AIDS, PNA, RD, jaundice, hypothermia, NEC, IUGR, first, and fifth-minute APGAR score, birth weight, gestational age, maternal age, and type of pregnancy were significantly associated with early mortality (p-value < 0.25). However, in the multi-variable Weibull regression model only Preeclampsia, PNA, RD, NEC, birth weight, and gestational age were significant predictors of early mortality (P-value < 0.05). In this study, LBW neonates born from a mother with preeclampsia had a 1.77 times higher risk of death than their counterparts. (AHR = 1.77; 95%CI: 1.32–2.36). LBW neonates with PNA had a 1.64 times higher risk of death than neonates without PNA (AHR = 1.64, 95%; CI: 1.14–2.36) by keeping other variables constant. Similarly, LBW neonates with RD had a 1.76 times higher risk of death

than LBW neonates without RDS (AHR = 1.76; (95% CI: 1.31–2.34)) holding other variables constant.

The hazard of death in LBW neonates with NEC was 2.78 times higher as compared with their counterparts (AHR = 2.78: 95% CI; 1.79–4.32). LBW neonates with birth weight less than 1000gm. and 1000–1499 gm. were three times and two times at high risk of death with (AHR = 3.13 ;(95% CI: 1.91–5.12)) & (AHR = 1.99; (95%; CI:1.47–2.68)) respectively holding other variables constant. The current study also showed that LBW early neonates who are preterm were 1.86 times (AHR: 1.86 ;(95% CI; 1.30–2.67)) at higher risk of death as compared to those of term neonates (Table 6).

Discussion

The overall aim of this study was to assess incidence and predictors of mortality among LBW neonates in the first week of life admitted to the NICU of Northwestern Ethiopia Comprehensive Specialized Hospitals. This study showed that at the end of the follow up 32.46% (95% CI 29.12% -35.8%) of LBW neonates died. This finding was in line with a study conducted in South Africa (32%) [22], and Brazil (29%) [19]. The possible reason could be both of the study areas where referral hospitals in which different complicated neonatal cases can be referred from different corners of the country. So, due to a high number of complicated cases, the mortality could be increased. On the other hand, this result was higher than a study conducted in Tanzania (5%) [45], and India 21.2% [21]. This marked difference might be attributed to NICU setup, differences in study design, and inclusion criteria. Those studies from other countries were conducted in a cross-sectional study design. The other reason is those studies include only inborn neonates, but the present study included both inborn and outborn neonates. However, the result of this study was lower than a study conducted in Saudi Arabia (41%) [46]. This difference might be due to the characteristics of the study participants, because they included only extremely low birth weight, and premature neonates [21].

In this study, the overall incidence of early neonatal mortality was 75.63 per 1000 neonate day observations (95% CI: 66.76–85.67). This finding was lower than a study conducted in Bangladesh with 112 per 1000 neonate day observations with (95% CI, 91–136) [47]. This variation might be due to the way of follow-up. Those studies start to follow from the time of birth and in their home up to the end of follow-up, but in the present study, the follow-up starts from admission to NICU and did not include neonates who died immediately after birth, and in their homes, so this may underestimate the overall incidence of ENM. In contrast to these, the finding of this study was higher than a study conducted in Brazil 52 per 1000 neonates [9], India 21.22 per 1000 live births

Table 5 Model comparisons among the Cox proportional hazard model and parametric Regression models using AIC, BIC, and LR criteria

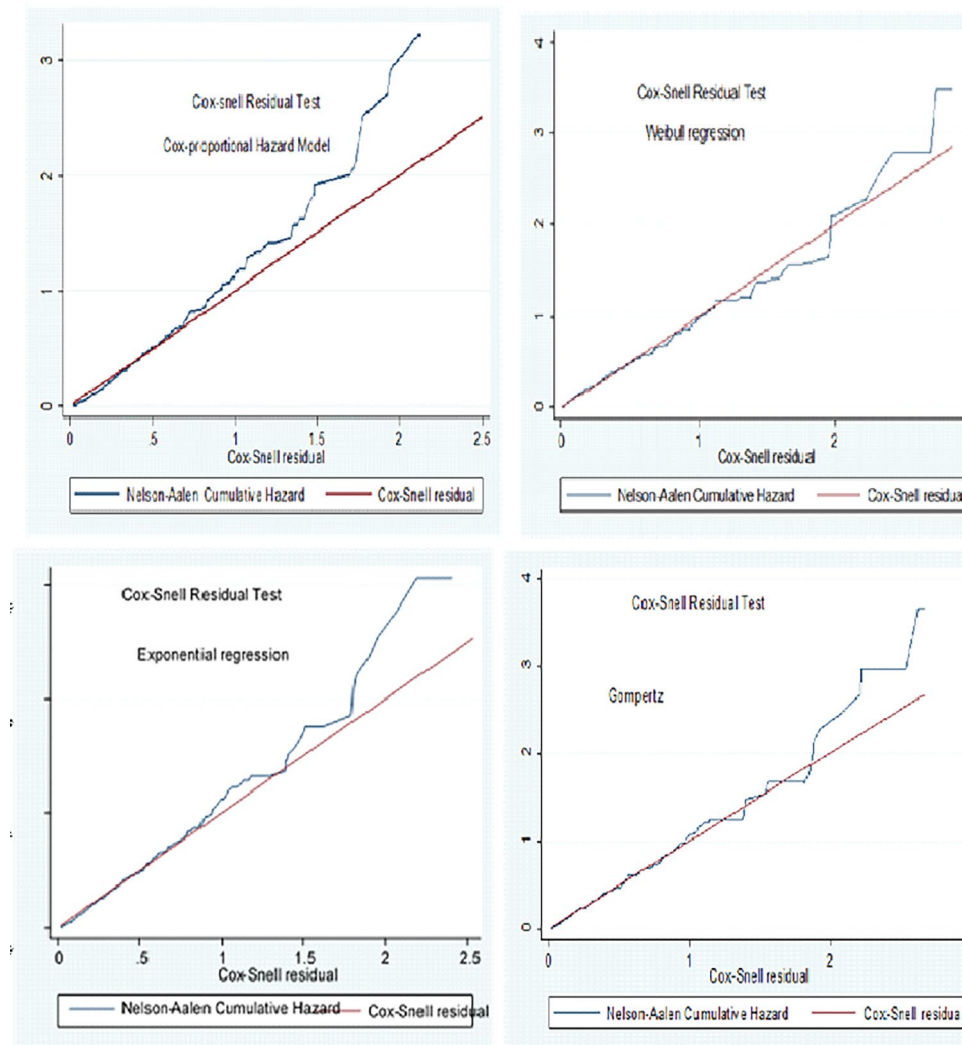| Model	Baseline hazard	Log-likelihood ratio	AIC	BIC
Cox regression	Unspecified	-1466.71	2977.42	3079.382
Weibull regression	**Weibull**	**-574.1256**	**1196.251**	**1307.482**
Exponential regression	Exponential	-585.0281	1216.056	1322.653
Gompertz regression	Gompertz	-582.7498	1213.5	1324.731

Fig. 3 The Cox-Snell residual test of Semi-parametric, and parametric Survival models

[10], Burkina Faso 1.93 per 1000 neonate /day (95% CI, 1.2–3.1) [11], and Bahir Dar 22.16 (95% CI14.14-34.75) per 1000 neonate day observation at the seventh day [12]. The variation between Brazil, Burkina Faso, and the present study might be due to differences in inclusion criteria, quality of service provision, and NICU setup differences. Those studies included LBW neonates who were not admitted, whereas the present study included only admitted neonates. Additionally, hospitals in Brazil and Burkina Faso may have more advanced care and service provision, and their NICU setup may be more advanced than hospitals of our study setting.

In this study, the incidence of mortality on the first day was high, with an incidence of 105.12 (95% CI; 84.44 -130.88) per 1000 neonate days' observation. This finding was nearly three times higher than a study conducted in Bahir Dar, Ethiopia 38 per 1000 neonate day observations [12]. The possible reason for this discrepancy might

be that, in the present study, the proportion of LBW neonates with RDS and LBW neonates from preeclampsia mothers was higher than a study conducted in Bahir Dar. Additionally, it could be due to differences in neonates' age that include only neonates who were in critical time (the first week of life). The other possible explanation might be related to pregnancy and birth-related complications that may result in a delay in the diagnosis and management of neonatal problems among early neonates.

Concerning predictors of mortality, this study identified several predictors of mortality. Accordingly, LBW neonates born from a mother with preeclampsia were nearly two times more likely to die than neonates whose mothers did not have preeclampsia. This result was consistent with a study done in Greece [34], and China [33]. This is due to a decrease in uteroplacental blood flow, and then, the neonates develop hypoxia and IUGR

Table 6 Bivariable and multivariable Weibull regression analysis for predictors of mortality among low birth weight neonates in their first week of life admitted to NICU of Northwestern Ethiopia Comprehensive Specialized Hospitals from March 21, 2020 to March 1, 2022. (n = 761)

Variables	Status		CHR(95%CI)	AHR(95%CI)
	Death	Censored		
Sex				
Male	118	277	0.83(0.65-1.065)	1.03(0.783–1.35)
Female	129	237	1	1
Maternal age				
≤20	39	66	1.2(0.86-1.72)	1.41(0.95–2.08)
≥35	28	91	0.67(0.45 – 1.00)	0.67(0.44–1.02)
21–34	180	357	1	1
Mode of delivery				
Instrumental	5	24	0.41(0.17–0.99) 0.99(0.75–1.34)	0 0.70(0.28–1.77)
CS	60	107	1	1.01(0.71–1.44)
SVD	182	383		1
Type of pregnancy				
Multiple	80	114	1.36(1.04–1.78)	1.15(0.86–1.55)
Single	167	400	1	1
Corticosteroid treatment				
No	176	400	0.83(0.63–1.09)	1.07(0.79–1.46)
Yes	71	114	1	1
Preeclampsia				
Yes	105	98	**2.23(1.73–2.87)**	**1.77(1.32–2.36)**
No	142	416	**1**	***
				1
APH				
Yes	29	42	1.40 (0.95–2.06)	1.38 (0.92–2.08)
No	218	472	1	1
Gravidity				
≤1	40	117	0.79(0.57–1.11)	0.82(0.57–1.20)
>1	207	407	1	1
HIV/AIDS				
Yes	21	18	1.72(1.10–2.69)	1.53(0.95–2.46)
No	226	496	1	1
1st minute APGAR				
<7	123	149	1.92 (1.49–2.46)	1.32(0.98-1.79)
≥7	124	365	1	1
5th minute APGAR				
<7	47	24	2.56(1.87–3.53)	1.40(0.95–2.08)
≥7	200	490	1	1
Birth weight				
≤999	23	10	**4.72(3.02–7.34)**	**3.13(1.91–5.12) ****
1000–1499	97	61	**3.22(2.47–3.4.20)**	**1.99(1.47–2.68)***
1500–2499	127	443	**1**	**1**
Gestational age				
<37	208	304	**2.6(1.85–3.66)**	**1.86(1.30–2.67)****
≥37	39	210	**1**	**1**
PNA				
Yes	47	40	**2.15(1.56–2.95)**	**1.64(1.14–2.36) ****
No	200	474	1	1
RDS				
Yes	167	189	**2.6(1.99- 3.40**	**1.76(1.31–2.34)***
No	80	325	**1**	**1**
Jaundice				
Yes	22	82	0.59(0.38-0.92)	0.81(0.50–1.29)
No	225	432	1	1

Table 6 (continued)

Variables	Status			CHR(95%CI)	AHR(95%CI)
	Death	**Censored**			
NEC					
Yes	26	20		**2.34(1.56–3.51)**	**2.78(1.79–4.32)***
No	221	494		1	1
Hypothermia					
Yes	101	168		1.21(0.94–1.57)	1.05(0.80–1.38)
No	146	346		1	1
IUGR		`			
Yes	19	22		1.52 (0.95–2.43)	1.58(0.95–2.61)
No	228	492		1	1

NB: ***=Significant variiable with p-value=0.00 &**=p-value≥0.001–0.05, 1=reference

which could increase the risk of dying [48]. Additionally, preeclampsia can be a threat to maternal life, and in this case, terminating the pregnancy could be mandatory, and therefore, the neonate would be delivered with immature organ systems, which increases the risk of death.

In addition, LBW neonates with perinatal asphyxia (PNA) had a higher risk of early death as compared with neonates without PNA. This result was consistent with studies done in Brazil [24], India, and Bangladesh [21, 23]. The possible reason for this could be the PNA contribut of the deprivation of oxygen in the body, which leads to progressive hypoxemia, and hypercapnia resulting in the central nervous system and other end-organ damage [42]. In the current study, the hazard of death among neonates with RDS was 1.76 times higher as compared with its counterpart. This finding was in line with a study conducted in Brazil [49], Zimbabwe [25], India [21, 44], and Bahir Dar, Ethiopia [12]. Since the majority of neonates are premature, the problem of lung immaturity (lack of adequate surfactant) is a common phenomenon that leads to lung collapse, and respiratory failure [42]. Furthermore, it might be due to a lack of administration of antenatal corticosteroids to mothers before 37 weeks of gestation, lack of surfactant replacement therapy [50], and due to inadequate number and lack of trained personnel in the use of Nasal Continuous Positive Airway Pressure (CPAP). Similarly, the hazard of death among neonates with necrotizing enter colitis (NEC) was 2.78 times higher than neonates who did not have (NEC). This result is supported by a study conducted in Brazil [26], China [30], South Africa [31], and Bahir Dar, Ethiopia [12]. The reason for this could be the majority of the study participants were preterm, and all of them were LBW,these groups of neonates have immature gastrointestinal tract and immature defense mechanisms, so they are more susceptible to infection, and as the intestinal tracts colonize by microbes it could easily perforate and develops peritonitis [42]. In addition to the above reasons, neonates with NEC have intestinal necrosis and dehydration, and this may increase the chance of death. In the present study, neonates with birth weights, less

than 1000 g and 1000–1499 g had three times and two times, higher risk of death as compared with neonates with a birth weight of 1500 to 2499.9 g respectively. This finding was consistent with studies conducted in Brazil [19], India [21], Bahir Dar, Ethiopia [12], and southern Ethiopia [16]. The possible justification for this could be, as birth weight decreases the risk of exposure to infection, hypothermia, and hypoglycemia could increase, and this could lead to the death of neonates. The other possible reason might be, due to immaturity of the lung which causes RDS, and it could lead to death. Particularly the immune system of LBW neonates may not be fully developed and may not fight of infections, therefore, it increases the hazard of death.

In this study, the other predictor of mortality was prematurity, which increases the hazard of death nearly two times as compared with those LBW neonates with a gestational age of 37 week and above. This finding was consistent with studies conducted in Brazil [27, 51], Iraq [29], Burkina Faso [28], Zimbabwe [25], and Southern Ethiopia [16]. The possible reason for this could be premature neonates have difficulty in adaptation of the extra uterine environment, due to immaturity of the organ system, and they face many fatal neonatal problems. This problem could decrease the probability of survival [8, 42]. Additionally, this may be due to improper care and inadequate availability of medical services and equipment like surfactant therapy, and mechanical ventilators unlike in middle-income and high-income countries.

Limitation

This study was conducted using a secondary data source, important variables, such as maternal and paternal educational level, occupational status, nutritional status of the mother, and monthly income were missed. In addition to this, the present study was conducted in hospitals, where neonates who were in the community were not included, which may underestimate the mortality. On the other hand, only hospitalized (high-risk) neonates were included, and it may overestimate the mortality rate.

Conclusion

In conclusion, the incidence of early neonatal mortality in LBW neonates was incredibly higher than e the overall early neonatal mortality in Northwest Ethiopia (Amhara region), and it continues to be a major public health problem. The highest number of death were recorded on the first day of admission. Preeclampsia, PNA, RDS, NEC, Birth weight, and prematurity were independent predictors of mortality among LBW neonates in their first week of life in Northwest Ethiopia.

Therefore, the stakeholders better to give strong emphasis to ELBW & VLBW neonates. The health care provider and other stakeholders shall give more emphasis and critical care on the first day of admission. Special care and support shall be given to LBW neonates who have fatal comorbidities like PNA, NEC, RDS, and neonates born from preeclampsia mothers. Further more, health care providers shall give appropriate ANC and PNC care and also they shall educate the mother and should give advice to the caregivers to perform KMC and breastfeed exclusively. A longitudinal prospective study in each low birth weight category will be better to address important variables that are missed in a retrospective study and to address the true effect of predictor variables.

Abbreviations

AHR	Adjusted Hazard Ratio
ANC	Antenatal Care
APGAR	Appearance, Pulse, Grimace, Activity, Respiration
APH	Antepartum Hemorrhage
CSH	Comprehensive Specialized Hospital
ELBW	Extremely Low-Birth-Weight
ENM	Early Neonatal Mortality
FMoH	Federal Ministry of Health
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
IUGR	Intra-Uterine-Growth-Restriction
LBW	Low-Birth-Weight
NEC	Necrotizing Enterocolitis
NICU	Neonatal Intensive Care Unit
PNA	Perinatal Asphyxia
RDS	Respiratory Distress Syndrome
UoGCSH	University of Gondar Comprehensive Specialized Hospital
VLBW	Very Low-Birth-Weight

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Authors' contributions

WTW: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Visualization Writing and original draft, CAW: Methodology, Supervision, Validation, Visualization, Writing –reviewing& editing, KAZ: Supervision, Visualization, Writing – reviewing& editing. Finally, all authors read and approved the final draft of the manuscript.

Data Availability

The dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval and Consent to participate

Ethical clearance was obtained from the institutional review board of University of Gondar on behalf of the ethical review committee of the School of Nursing with (Ref.no SN/231/2014). Ethics approval was approved by the respective institutions confirming that all study protocols were approved by IRB of the School of Nursing, University of Gondar. The IRB of School of Nursing, has waved informed consent of the medical records of the neonates. Since the study was conducted by using appropriate information from patient's medical charts, it could not inflict any harm on the patients. So informed consent was impractical for this study. This is in line with the Helsinki Declaration which states that in "medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There would be impossible to obtain for such research or would pose a threat to the validity of the research. In such situations, the research may be done only after consideration and approval of the research ethics committee". A letter of cooperation was written to the respective comprehensive Specialized Hospitals of Northwest Ethiopia, and permission was obtained from Clinical directors and relevant departments. At the time of data collection personal identifiers (name, medical registration number) were excluded. The confidentiality of the data was strictly maintained throughout the study process.

Consent for publication

Not applicable.

Conflict of Interest

The author declares that they have no conflict of interest.

Competing interests

The authors declare no competing interests.

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References

1. United Nation International Childrens Emergency Fund (UNICEF). 2021. neonatal mortality. [Available from: https://data.unicef.org/topic/child-survival/neonatal-mortality/.
2. Oza S, Lawn JE, Hogan DR, Mathers C, Cousens SNJBWHO. Neonatal cause-of-death estimates for the early and late neonatal periods for 194 countries: 2000–2013. 2014;93:19–28.
3. World health organization (WHO) LOW BIRTH WEIGHT. 2019 [Available from: https://www.who.int/data/nutrition/nlis/info/low-birth-weight.

4. Blencowe H, Krasevec J, De Onis M, Black RE, An X, Stevens GA et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. 2019;7(7):e849–e60.
5. World Health Organiization(WHO). Stanndards for improving the quality of care for small and sick new born in health facilities. 2020 [Available from: https://www.who.int/publications/i/item/9789240010765.
6. UNICEF. 1 in 7 babies worldwide born with a low birthweight – 2019, [Available from: https://www.unicef.org/press-releases/1-7-babies-worldwide-born-low-birthweight-lancet-global-health-unicef-who.
7. Tran HT, Doyle LW, Lee KJ, Graham SM. A systematic review of the burden of neonatal mortality and morbidity in the ASEAN Region. WHO South-East Asia Journal of Public Health. 2012;1(3):239–48.
8. Gebremeskel AT, Fantaye AW, Faust L, Obegu P, Yaya S. Gender differences in survival among low birthweight newborns and infants in sub-saharan Africa: a systematic review. Int Health. 2021;14(2):122–31.
9. Gaíva MAM, Lopes FSP, Ferreira SMB, Mufato LFJREE. Neonatal deaths of low birth weight newborns. 2018;20.
10. Pabbati J, Subramanian P, Renikuntla MJIJCP. Morbidity and mortality of low birth weight babies in early neonatal period in a rural area teaching hospital. Telangana India. 2019;6(4):1582.
11. Coulibaly A, Baguiya A, Millogo T, Meda IB, Koueta F, Kouanda S. Predictors of mortality of low birth weight newborns during the neonatal period: a cohort study in two health districts of Burkina Faso. Int J Gynaecol Obstet. 2016;135(Suppl 1):89–s92.
12. Woelile TA, Kibret GT, Workie HM, Amare AT, Tigabu A, Aynalem YA et al. Survival Status and Predictors of Mortality Among Low-Birth-Weight Neonates Admitted to the Neonatal Intensive Care Unit at Felege Hiwot Comprehensive Specialized Hospital, Bahir Dar, Ethiopia, 2020. 2021;12:451.
13. Federal Ministery of Health(FMOH). Ethiopian demographic health survey. Addis Ababa, Ethiopia.2016.
14. Federal Ministery of Health (FMOH) E. National Strategy for Newborn and Child Survival in Ethiopia. In: Maternal and Child Health DirectorateFederal Ministry of Health, editor. Addis Ababa, Ethiopia.2015.
15. Ethiopian Public Health Institute (EPHI). Ethiopian mini demographic and Health survey 2019. May; 2021.
16. Eshete A, Alemu A, Zerfu TAJI. Magnitude and risk of dying among low birth weight neonates in Rural Ethiopia: a community-based cross-sectional study. 2019;2019.
17. Dessu S, Habte A, Mesele MJP. The Kaplan Meier estimates of mortality and its predictors among newborns admitted with low birth weight at public hospitals in Ethiopia. 2020;15(9):e0238629.
18. Kebede BF, Genie YD, Zerihun MS, Beyene DT. Morbidity and mortality pattern of Preterm Low Birth Weight Neonates admitted in Amhara Region Refferal Hospitals of Ethiopia Retrospective Follow-Up study. 2021.
19. de Castro ECM, Leite ÁJM, de Almeida MFB, Guinsburg R. Perinatal factors associated with early neonatal deaths in very low birth weight preterm infants in Northeast Brazil. BMC Pediatr. 2014;14(1):312.
20. Castro EC, Leite ÁJ, Almeida MF, Guinsburg R. Perinatal factors associated with early neonatal deaths in very low birth weight preterm infants in Northeast Brazil. BMC Pediatr. 2014;14:312.
21. Pabbati J, Subramanian P, Renikuntla M. Morbidity and mortality of low birth weight babies in early neonatal period in a rural area teaching hospital, Telangana, India. 2019.
22. Michaelis IA, Krägeloh-Mann I, Manyisane N, Mazinu MC, Jordaan ER. Prospective cohort study of mortality in very low birthweight infants in a single centre in the Eastern Cape province, South Africa. BMJ Paediatrics open. 2021;5(1):e000918.
23. Bari M, Ullah M, Khatun MJTJTA. Morbidity and mortality of low birth weight baby. 2008;21(1):35–9.
24. de Almeida MF, Moreira LM, Vaz dos Santos RM, Kawakami MD, Anchieta LM, Guinsburg R. Early neonatal deaths with perinatal asphyxia in very low birth weight brazilian infants. J Perinatology: Official J Calif Perinat Association. 2015;35(11):954–7.
25. Zvenyika-Hlatywayo L, Chimhuya S, Gumbo FJCPR. Risk factors for mortality in low birth weight infants at Harare hospital (maternity unit). Zimbabwe. 2018;2(1):33–41.
26. Guinsburg R, de Almeida MFB, de Castro JS, Silveira RC, Caldas JPS, Fiori HH, et al. Death or survival with major morbidity in VLBW infants born at brazilian neonatal research network centers. J Maternal-Fetal Neonatal Med. 2016;29(6):1005–9.
27. Cetinkaya SE, Okulu E, Soylemez F, Akin İM, Sahin S, Akyel T et al. Perinatal risk factors and mode of delivery associated with mortality in very low birth weight infants. 2015;28(11):1318–23.
28. Coulibaly A, Baguiya A, Millogo T, Meda IB. Kouanda SJIJoG, Obstetrics. Predictors of mortality of low birth weight newborns during the neonatal period: a cohort study in two health districts of. Burkina Faso. 2016;135:89–S92.
29. Hassan BAKAJT-QMJ. Neonatal death in low Birth Weight Infants in Basrah Maternity & Children Hospital at 2008. 2017;14(2).
30. Qian T, Zhang R, Zhu L, Shi P, Yang J, Yang C-y et al. Necrotizing enterocolitis in low birth weight infants in China: mortality risk factors expressed by birth weight categories. 2017;58(6):509–15.
31. Ballot DE, Chirwa T, Ramdin T, Chirwa L, Mare I, Davies VA, et al. Comparison of morbidity and mortality of very low birth weight infants in a Central Hospital in Johannesburg between 2006/2007 and 2013. BMC Pediatr. 2015;15:20.
32. Sadeghi Moghaddam P, Aghaali MJSE-MJ. Survival of 798 low birth weight infants according to birth weight and gestational age. 2015;16(11–2).
33. Abbas K, Begum N, Ahmed Z, Mubarik S, Haq IU, Ghulam N et al. Low birth weight, and low ponderal index mediates the association between pre-eclampsia, placenta previa, and neonatal mortality. 2020;49(4):654.
34. Chatziioannidis I, Mitsiakos G, Karagianni P, Tsakalidis C, Dimopoulou AJJP, Medicine NI. Predictors of early neonatal mortality in extremely low birth weight infants in a neonatal intensive care unit over a 10-year period. 2020;9(1):e090115–e.
35. Federal Ministery of Health (FMOH). Ethiopian,Mini demographic health survey. Ethiopia: Addis Ababa; 2019.
36. World Health Organization(WHO). New born mortality 2020 [Available from: https://www.who.int/news-room/fact-sheets/detail/levels-and-trends-in-child-mortality-report-2021.
37. World health organization W. Global nutrition targets:Low birth weight, 2014 [Available from: https://www.who.int/publications/i/item/WHO-NMH-NHD-14.5.
38. United Nation. Sustainable development goal. 2018.
39. Federal minister of health (FMOH). PROFILE OF PRETERM AND LOW BIRTH WEIGHT PREVENTION AND CARE,. Addis Ababa.Ethiopia.2015.
40. Ministry of Health E. Health Sector Transformation Plan-II. 2021.
41. Lehtonen L, Gimeno A, Parra-Llorca A, Vento M. Early neonatal death: a challenge worldwide. Semin Fetal Neonatal Med. 2017;22(3):153–60.
42. Federal Ministry of Health Ethiopia. Neonatal intensive care unit (NICU) training participants' manual. Ethiopia: Addis Ababa; 2021.
43. Castro ECMd, Leite ÁJM, Guinsburg RJRPP. Mortality in the first 24 h of very low birth weight preterm infants in the Northeast of Brazil. 2016;34:106–13.
44. Gupta S, Adhisivam B, Bhat BV, Plakkal N, Amala R. Short term outcome and predictors of Mortality among very low Birth Weight Infants - a descriptive study. Indian J Pediatr. 2021;88(4):351–7.
45. Kibona SE, Sungwa EE, Dika HI, Laisser RM, Mhada T, Malale KN et al. Immediate Seven Day Outcomes and Risk factors of low Birth Weight Neonates at Referral Hospitals in Mwanza City, Tanzania in October 2020. 2021;34(4):451–63.
46. Abolfotouh MA, Al Saif S, Altwaijri WA, Al Rowaily MA. Prospective study of early and late outcomes of extremely low birthweight in Central Saudi Arabia. BMC Pediatr. 2018;18(1):280.
47. Yasmin S, Osrin D, Paul E, Costello AJBWHO. Neonatal mortality of low-birth-weight infants in Bangladesh. 2001;79:608–14.
48. Backes CH, Markham K, Moorehead P, Cordero L, Nankervis CA, Giannone PJ. Maternal preeclampsia and neonatal outcomes. J Pregnancy. 2011;2011:214365.
49. Guinsburg R, de Almeida MFB, de Castro JS, Silveira RC, Caldas JPS, Fiori HH et al. Death or survival with major morbidity in VLBW infants born at brazilian neonatal research network centers. 2016;29(6):1005–9.
50. TASKER KLIEGMANSBLUM, WILSON,,. Nelson Text book of pediatrics. 21th Edition. ed2021.
51. Gaiva MAM, Fujimori E, Sato APSJREEU. Neonatal mortality in infants with low birth weigh. 2014;48:778–86.

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