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Research Article

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Time to Death and its Predictors Among Low-Birth Weight Neonates Admitted in Addis Ababa, Ethiopia

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Abstract

Background

Globally, low birth weight is one of the neonatal problems, which account approximately 80% of all newborn deaths, ranges from 68 deaths per 1000 live births to 83 deaths per 1000 live births. The problem is especially high in developing countries including Ethiopia. To tackle this critical neonatal problem, identifying the hazard time to death and its predictors is crucial. Therefore, this study aimed to investigate time to death and predictors of mortality among low-birth-weight neonates admitted at Addis Ababa governmental hospitals in Ethiopia, 2021.

Methods

A retrospective cohort study was employed among 329 neonates with LBW admitted in neonatal intensive care unit of selected four governmental hospitals in Addis Ababa, between January 2018 and January 2021. Epi-data version 7.2.2.6 and SPSS version 25 was used to data entry and analysis respectively. Kaplan Meier survival curve was used to estimate the cumulative survival time. A log rank test was used to compare the probability of hazard among variables. Bi-variable and multivariable cox proportional hazards models were used to identify predictors and variables having p value < 0.05 were considered as statistically significant. Results were presented using text, figure and tables.

Result

In this study 105 (31.9%) neonates were died with incidence rate of 40.1 (95%CI: (95%CI: 33.24, 48.74) per 1000-person day. Extreme very low birth weight (AHR: 2.14; 95%CI: 1.06, 4.30), apnea (AHR: 3.04; 95%CI: 1.87, 4.94), asphyxia (AHR: 2.34; 95%CI: 1.04, 5.26), unable to get only breast-feeding (AHR: 8.74; 95%CI: (5.26-14.57) and lack of kangaroo mother care (AHR: 8.86; 95%CI: 1.15, 68.52) are significant predictors of time to death.

Conclusion and Recommendations

The incidence of death was higher compared to other previous studies with median survival time of 18days. Being extremely very low-birth-weight, apnea, asphyxia, kangaroo mother care and exclusive breast feeding were found to be a predictors for time to death. Therefore, intervention on the identified predictors could be so important to improve the survival status of low-birth-weight neonates.

Key words: Time to Death, Low Birth-Weight Neonate, Addis Ababa

1. Introduction

World Health Organization (WHO) defines low birth weight (LBW) as newborns weighing < 2,500 gram, in the first hours of life, with further categorization of very low birth weight (VLBW <1500 g) and extremely low birth weight (ELBW <1000 g) [1]. Low birth weight can affect nearly every organ in the body including:- respiratory system, central nervous system, gastrointestinal system, genito urinary system and cardiac functions leads to problems with their lungs, intestinal tract, vision and hearing, and future develop- mental delays [2,3]. It is a complex syndrome that includes preterm neonates, small for gestational age neonates at term and the overlap between these two situations – preterm, small for gestational age neonates, who typically have the worst outcomes [4]. However, many socio demographic, obstetric, medical and nutritional factors have their own impact on neonates weight among them infant sex, racial/ethnic origin, pre-pregnancy maternal weight and height, high blood pressure, multiple gestation parity, history of prior

low-birth-weight infants, gestational weight gain and caloric intake, general morbidity and episodic illness, malaria, cigarette smoking, alcohol consumption and tobacco chewing are risk factors of delivering LBW neonate [3,5].

Globally there were more than 20.5 million LBW neonates in 2015, and more than 96% of LBW newborns were born in South-central Asia and Africa [6]. LBW accounts for approximately 80% of all newborn deaths, it has been shown that the mortality range can vary 100-fold across the spectrum of birth weight and rises continuously with decreasing weight [6]. Low birth weight newborns have a higher risk of death in the first 28 days of life [6]. Low birth-weight newborns health care costs higher than normal birth weight newborns because LBW newborns need special care in the hospital after birth. They may need help with breathing, staying warm, protection against infection, and getting enough nutrition [3].

LBW is among the strongest predictors of infant morbidity and mortality in most parts of the developing world. Epidemiological observations show that infants weighing less than 2,500 gm are approximately 20 times more likely to die than normal birth weight babies are, more common in developing than developed countries [7]. The mortality rate among LBW neonates in Ethiopia significantly vary between different study areas and ranges from 68 deaths per 1000 live births to 83 deaths per 1000 live births [8,9]. Those who survive are more likely to suffer consequences of LBW, low birth weight due to restricted fetal growth affects the person throughout life and is associated with poor growth in childhood and a higher incidence of adult diseases, such as stunted growth, lower IQ, type 2 diabetes, hypertension and cardiovascular disease. An additional risk for girls is having smaller babies when they become mothers [10].

WHO launches a strategy mentioned as Global Nutrition Targets 2025: LBW policy brief to achieve a thirty percent reduction in the number of LBW new- born by the year 2025. This policy will be achieved through intensive follow up of the neonates admitted with low birth weight and appropriate health interventions through determining the time that neonate will die [4]. Many countries of the world including Ethiopia is not on track to meet the WHA global target on low birth weight [6]. Even though there are significant improvements by the number of neonatal intensive care units for the last few years in Ethiopia, instead of decreasing up on time, the neonatal mortality was increased from 29 per 1000live birth in 2016 to 30 per 1000live birth in 2019(11,12).

The survival of LBW neonates depends on many factors like economic, socio- demographic, maternal medical, obstetric, and clinical factors. But predictors of mortality among LBW neonates in Ethiopia were inconsistently reported by fragmented studies conducted in different study areas [13,14]. To give appropriate health care and to achieve sustainable development goal, survival status of LBW neonates have to be identified and recent information is needed. Therefore, this study aimed to investigate recent and representative data on predictors of mortality among low-birth-weight neonates admitted at Addis Ababa governmental hospitals in Ethiopia, 2021.

2. Methods

2.1 Study Area, Design and Study Period

The study was conducted in Addis Ababa which is the capital city of Ethiopia and seat of African Union & Economic Commission for Africa. Addis Ababa has a population size of over 3 million (3038096) with yearly growth rate of 2.1(data obtained from central statistics agency of Ethiopia). Addis Ababa is located between 8055° and 9005° North Latitude and between 38040° and 38050° East Longitude and the total Land area is 54,000 hectares. It is established on November, 1887 by Emperor Menelik II and Empress Tayitu. Its average elevation is 2,500 meters above sea level, and hence has a fairly favorable climate and moderate weather conditions [15]. The city has 12 governmental hospitals, five hospitals owned by Addis Ababa health bureau, four by federal ministry of health (FMOH), one by ministry of education (Addis Ababa University), two by defense force according to Addis Ababa health office. Therefore, this institutional based retrospective cohort follow up study was conducted in randomly selected hospitals which are Tikur Anbessa Specialized hospital, Gandhi memorial hospital, Zewditu hospital and Yekatit12 hospital medical college from March 15, 2021 to April 15, 2021 G.C.

3. Population

All low-birth-weight neonates admitted in neonatal intensive care unit (NICU) at selected public hospitals of Addis Ababa are sources of population and all low-birth-weight neonates admitted to NICU of selected public hospitals in Addis Ababa from January 2018 to January 2021 were study population.

3.1 Inclusion and Exclusion Criteria

All records of LBW neonates admitted in selected governmental hospitals of Addis Ababa neonatal intensive care unit were included, while records of LBW neonates with incomplete information (absence of admission date, censored date, and unknown outcome) were excluded from the study.

3.2 Sample Size and Sampling Procedure

The sample size for the first objective (death as outcome of LBW treatment) was determined by using single population formula by considering the following statistical assumptions. P = proportion of mortality among LBW neonates 8.3%, from study done in Arba Minch General Hospital(9), Z α/2 = the corresponding Z score of 95% CI, d= Margin of error (5%) and N= Sample size n = 113, Adding 10 % contingency rate for an incomplete chart makes the final sample size 124.

$$n = \frac{(Z_{\frac{\alpha}{2}})^2 \times p(1-p)}{(d)^2}$$

For the second objective (predictor variables of mortality), the sample size was determined using Stata with a consideration of hazard ratio from the previous different studies. From these ANC follow up with (AHR:2.67) was the one highest sample size of 329 [16]. The study was conducted in Addis Ababa governmental hospitals. Among the hospitals, 30% or four

hospitals were selected by using simple random sampling method, which were Black lion hospital, Yekatit 12 hospital, Zewditu hospital and Gandhi memorial hospital and totally, 5598 admitted LBW neonates. Then the total number of selected LBW newborns from each hospital was 91 from BLH, 78 from Yekatit hospital, 100 from Gandhi memorial hospital and 60 from Zewditu hospital by using proportional allocation formula. Finally, the study subjects were selected by using systematic random sampling technique from a total sampling frame of 5598, the first participant/chart was selected randomly by lottery method, the other study participants/chart was selected every K = 17 interval.

4. Study Variables

The outcome variable for this study was **time to death** coded as (death=1, and censored=0). Independent variables include: - **socio-demographic factors** (maternal age and residence), **maternal behavioral factors** (alcohol intake Smoking and Chat chewing), **maternal medical factors** (history of maternal DM, HIV/AIDS, syphilis, iron deficiency anemia, pregnancy induced hypertension, UTI, STI, intra-partum fever and any medication intake), **maternal obstetrical factors** (ANC visit, gravidity, parity, history of small baby, history of abortion, history of preterm delivery, mode of delivery, place of delivery and multiple pregnancy), **neonatal factors** (sex, birth weight, gestational age, admission diagnosis, APGAR score, resuscitation at birth and post-natal age).

4.1 Operational Definitions/ Definition of Terms

Survival:- The act or fact of living LBW neonate despite LBW related death during hospitalization period, **Died:-** LBW neonate that has died while s/he was in the in-patient care and death report is recorded in patient card, **Defaulted**:- LBW neonate cases that are sign (parents on behalf of their child) against treatment to leave treatment before cure, **Medical transfer**:- LBW neonate is referred to other health facilities for medical reasons, **Censored**:- LBW neonates who did not develop the outcome of interest (death) until the end of follow-up period, those lost to follow-up or transfer out to a different care unit during the study period.

5. Data Collection Tool and Procedure

Data abstraction sheet was used to assess survival status and predictors of LBW. The abstraction sheet was prepared in English by reviewing relevant literature to the problem under study to include all possible variables that address the objective of the study [17]. The abstraction sheet contains socio demographic factors, maternal obstetric factors, maternal medical factors and neonatal factors. Data quality was assured by giving one day training for supervisor and card reviewers to improve the skill of data collectors and to ensure the consistency of the data extraction tool. Orientation was given to the supervisor separately on how to supervise the data collectors, check for completed data abstraction checklist and correct any problem. Data extraction forms were checked before data collection. Completeness of the collected data was checked daily basis during data collection and given prompt feedback by the supervisor and the principal investigator. Besides this, the principal investigator carefully entered and thoroughly cleans the data before the commencement of the analysis. Pretest was done on 5% of the study samples in Menelik II Memorial Hospital before one week of the actual data collection, Addis Ababa where it is assumed to have similar characteristics to the study area, after the pretest necessary corrections were done on the check list. To collect the study participant's total LBW caseload was assessed in the data based on the electronic system from the catalog of admitted neonates in NICU wards of selected four hospitals. Then medical registration number (MRN) of all neonates was sorted. After this, simple random method was applied to select the study participants. Finally, the selected medical registration charts were picked out from the medical card registration room and data collection started. Data was collected by two master's students and the supervisor was also master student in Epidemiology, the starting point for retrospective follow-up was the time of admission and the end point was date of discharge, date of death, date of lost to follow up and date of transfer out.

6. Data Processing and Analysis

The collected data was coded and entered and cleaned in Epi data version 7.2.2.6 then transported to SPSS version 25 (Statistical Package for the Social Sciences) for analysis. n

The Kaplan Meier survival curve was used to estimate survival probability of LBW neonates after admission at different time intervals. Kaplan Meier survival curve together with log rank test were used to check the presence of difference in survival among categories of covariates and log rank test was used to compare survival curves. Model fitness was tested by using Schoenfeld residuals test for proportional assumption and it was fitted with a total global test result of 0.2827. Cox regression was carried out to find predictors of survival status. Bi-variable cox regression was first fitted and those independent variables which became significant on the bi-variable cox regression having p-value ≤ 0.005 level of significance were included in the multivariable analysis. Cox proportional-hazard regression was fitted at 5% level of significance to determine the net effect of each explanatory variable on time to death after admission (Hazard ratio with its 95% confidence interval and p-value was used to measure strength. Variable with P-value < 0.05 were considered as statistically significant predictors. Finally, the results of the study were presented with text, graph, table and figure.

7. Result

7.1 Socio-Demographic and Behavioral Related Predictors

In this study a total of 329 neonates admitted with low birth weight were involved. Among them, 105(31.9%) neonates were died. Majority of 286(86.9%) neonates come from urban areas, of which male accounts 181(55%) of admitted low birth weight newborns and which contributed 61(58.1%) of died neonates. More than four fifth 93(88.6%) of died neonates was admitted in the age of <24hour 298(90.6%). The mean age of mothers found to be 26.30±4.60SD years old, majority of 269(82%) them are belonging to age group 35-49 years old and most of 86(81.9%) neonatal death was concentrated in this age group of mothers.

Chewing chats, alcohol intake and smoking history of all mothers was not recorded. In considering blood group and RH 142(43%) of mothers and 125(38%) of newborns blood group was O+ and 91(27.6%) mothers and 111(33.8%) of newborns blood group and RH was A+.

7.2 Maternal Medical Related Predictors

Among the total mothers enrolled in the study 35(10.6%) of the mothers had a history of chronic disease, more than two third them had HIV/AIDS 13(37%), hypertension 8(23%) and diabetic 7(20%) cases. The results of this study also indicated that 7(2.1%) mothers had a family history of chronic disease.

7.3 Maternal Obstetric Related Predictors

Among the total mothers enrolled in the study 196(60%) of them gave birth through spontaneous vaginal delivery and majority of 309(94%) them had more than four ANC follow-up. Around half of 160(48.6%) mothers have primi-gravida and they contribute for more than half 55(52.4%) of newborns death. Majority of 321(97%) mothers had delivered at health institution and it was attended by health professionals. Of the 105 who died, more than half 55(52.9%) and more than one fourth 27(25.7%) neonates were died from mothers who didn't take antenatal steroids and mothers with history of abortion respectively. 263 (80%) of mothers had singleton pregnancy and contributed for nearly three fourth (75.2%) of neonatal deaths.

Above half (57.8%) of mothers had obstetric complications like preeclampsia 75(22%), history of preterm delivery 15(4.6%), history of still birth 6(1.8%) and history of small baby 16(4.9%) were identified (Table 1).

Variables	Categories	Total (%)	Status of the newborn	
			Died (%)	Survived (%)
ANC follow-up	Yes	318(96.7%)	101 (96.2%)	217 (96.9%)
	No	11(3.3%)	4 (3.8%)	7 (3.1%)
How many ANC follow-up	≥Four	309(93.9%)	99 (94.3%)	210 (93.8%)
	Three times	3(0.9%)	1 (1%)	2 (0.9%)
	Twice	5(1.5%)	1 (1%)	4 (1.8%)
	Once	1(0.3)	0 (0%)	1 (0.4%)
	No ANC follow-up	11(3.3%)	4 (3.8%)	7 (3.1%)
Place of delivery	1	1.8%	9.236	
	Health institution	321(97.6%)	101 (96.2%)	220 (98.2%)
	Home	8(2.4%)	4 (3/8%)	4 (1.8%)
Gravidity	One	160(48.6%)	46 (43.8%)	114 (50.9%)
	2-4	155(47.1%)	55 (52.4%)	100 (44.6%)
	>4	14(4.3%)	4 (3.8%)	10 (4.5%)
History of abortion	Yes	69(21.0%)	27 (25.7%)	42 (18.8%)
	No	260(79%)	78 (74.3%)	182 (81.3%)
Iron/folic acid intake	Yes	312(94.8%)	97 (92.4%)	215 (96%)
	No	13(4%)	6 (5.7%)	7 (3.1%)
	Unknown	4(1.2%)	2 (1.9%)	2 (0.9%)
Anti-natal steroids intake	Yes	82(24.9%)	30 (28.8%)	52 (23.3%)
	No	174(52.9%)	55 (52.9%)	119 (53.4%)
	Unknown	71(21.6%)	19 (18.3%)	52 (23.3%)
TT vaccine intake	Yes	312(94.8%)	97 (92.4%)	215 (96%)
	No	12(3.6%)	5 (4.8%)	7 (3.1%)
	Unknown	5(1.6%)	3 (2.9%)	2 (0.9%)
Mode of delivery	SVD	196(59.6%)	72 (68.6%)	124 (55.4%)
	C/s	130(39.5%)	33 (31.4%)	97 (43.3%)
	Instrumental	3(0.9%)	0 (0%)	3 (1.3%)
Type of pregnancy	Single	263(78.0%)	79 (75.2%)	184 (82.1%)
	Twin	60(18.2%)	23 (21.9%)	37(16.5%)
	Triple	6(1.8%)	3 (2.9%)	3 (1.3%)
Obstetric complications	Yes	190(57.7%)	56(53.3%)	134(59.8%)
	No	139(42.2%)	49(46.7%)	90(40.2%

Preeclampsia	Yes	75(22.8%)	19 (18.1%)	56 (25%)
	No	254(77.2%)	86 (81.9%)	168 (75%)
PROM	Yes	53(16.1%)	14 (13.3%)	39 (17.4%)
	No	276(83.9%)	91 (86.7%	185 (82.6%)
Bleeding during pregnancy	Yes	17(5.2%)	8 (7.6%)	9 (4%)
	No	312(94.8%)	97 (92.4%)	215 (96%)
IUGR	Yes	20(6.1%)	5 (4.8%)	15 (6.7%)
	No	309(93.9%)	100 (95.2%0	209 (93.3%)

Table 1: Maternal Obstetric Factors of Neonates with Low Birth-Weight and Their Mothers at Nico of Governmental Hospitals in Addis Ababa Ethiopia, 2021.

7.4 Neonatal Related Predictors

Among the newborns delivered at health institution 51(15.5%) of newborns were resuscitated at birth and 250(76%) and 116(35%) of them had less than seven APGAR score at first and fifth minute respectively. Newborns who initiate EBM in one hour after birth and who kept in KMC are contributed for only one tenth (11%) and 1(1%) of the low-birth-weight mortality.

The study finding shows that among the total enrolled neonates, majority of 296(90%) newborns were categorized under preterm or less than 37 weeks gestational age and three fourth 247(75%) of them were developed new diagnosis during follow-up time. The common medical problems identified during the study period were hypothermia 227(69%), hypoglycemia 111(34%), anemia 48(16%), HAI 30(9%), LONS 10(3%), meningitis 8(2.4%) and polycythemia 6(1.8%). From which 78(74.3%), 41(39%), 25(23.8%), 10(15.2%), 3(2.9%), 3(2.9%) and 2(1.9%) of them were died during the follow-up period respectively. The other common cause of admission and medical problems developed during follow-up time were EONS, RD, asphyxia, neck, DIC, DHN, apnea and neonatal jaundice (Table 2).

Variables	**Category**	**Total (%)**	**Status of newborn**	
			Died (%)	**Survived (%)**
Cry immediately after birth	Yes	258(78.4%)	66 (62.9%)	192(86.1%)
	No	53(16.1%)	31 (29.5%)	22 (9.9%)
	Unknown	17(5.2%)	8 (7.6%)	9 (4%)
Resuscitated at birth	Yes	51(15.5%)	30 (28.6%)	21 (9.4%)
	No	278(84.5%)	75 (71.4%)	203(90.6%)
1st minute APGAR score	<7	250(76%)	87 (90.6%)	163(77.3%)
	>7	57(17.3%)	9 (9.4%)	48 (22.7%)
5th minute APGAR score	<7	116(35.2%)	53 (55.2%)	63 (55.2%)
	>7	191(58.1%)	148(44.8%)	43 (70.1%)
Keep in KMC	Yes	26(8.0%)	1 (1%)	25 (11.2%)
	No	303(92%)	104 (99%)	199(88.8%)
Only EBM feeding during follow-up	Only EBM	255(77.5%)	47 (44.8%)	208(92.9%)
	With additional food	74(22.5%)	58 (55.2%)	16 (7.1%)
Gestational age	<37 weeks	296(90.0%)	100(95.2%)	196(87.5%)
	37-41 weeks	30(9.1%)	5(4.8%)	25(11.2)
	≥42 weeks	3(0.9%)	0(0%)	3(1.3%)
Birth weight	<1000 gram	31(9.4%)	26(24.8%)	5(2.2%)
	1000-1500 gram	112(34.0%)	47(44.8%)	65(29%)
	1500-2500 gram	186(56.5%)	32(30.5%)	154(68.8%)
Asphyxia	Yes	61(20.6%)	35 (33.3%)	26 (11.6%)
	No	268(81.4)	70 (66.7%)	198(88.4%)
EONS	Yes	229(70%)	79 (75.2%)	150 (67%)
	No	100(30%)	26 (24.8%)	74 (33%)
RD	Yes	212(64%)	87 (82.9%)	125(55.8%)
	No	117(36%)	18 (17.1%)	199(44.2%)

Prematurity	Yes	233(71%)	86 (81.9%)	147(65.6%)
	No	96(29%)	19 (18.1%)	77 (34.4%)
SGA	Yes	86(26.1%)	22 (21%)	64 (28.6%)
	No	243(73.9%)	83 (79%)	160 (71.4%
DHN	Yes	97(29.5%)	38 (36.2%)	59 (26.3%)
	No	232(70.5%)	67 (63.8%)	165(73.7%)
DIC	Yes	10(3.0%)	8(7.6%)	2(0.9%)
	No	319(97.0%)	97(92.4%)	222(99.1%)
Neck	Yes	28(8.5%)	20 (19%)	8 (3.6%)
	No	301(91.5%)	85 (81%)	216(96.4%)
Apnea	Yes	64(19.4%)	53 (50.5%)	11 94.9%)
	No	265(80.6%)	52 (49.5%)	213(95.1%)
CPAP	No	156(47.4%)	84(80.0%)	72(37.1%)
	Yes	173(52.6%)	21(20.0%)	152(67.9%)

7.5 The Newborns Survival Status

329 newborns admitted to NICU have followed for 28days. The overall mean survival time was 17.76 days (95%CI: 16.25, 19.30), the median time was 22days and the 50th percentile was 22.00 days. In this study 105(31.9%) of the study participant were died during the follow-up period and from these male accounts, the higher value 58.1%. Among the total neonates included in this study, 224 (68.1%) were censored of which 188(57.1%) discharged to home, twelve (3.7%) transfer out, 7(2.1%) lost from follow-up, one (0.3%) left against medical advice and 16(4.9%) neonates' outcome was not known because of completed follow up period without known outcome. The total extent of follow-up was 2608 person-day, with an incidence rate of 40.25 deaths per 1000 person-day observation (95%CI: 33.24, 48.74). This study shows that 16(12.4%) low-birth-weight neonatal deaths during the first 24 hours and 27(25.7%) in the first 48 hours with incidence rate of 48.9 deaths per 1000 live births with standard error of 0.01(95%CI; 0.03, 0.78) and 89.9 deaths per 1000live births with standard error of 0.01(95%CI; 0.06, 0.13) respectively.

7.6 Overall Survival Function (survivorship function)

The overall Kaplan- Meier estimate showed that the probability of survival of low birth-weight neonates was highest in the first day of admission, which relatively falls as follow up time increases. During the first day of hospital stay, a maximum (95.1%) cumulative proportion of surviving was observed with a standard error of 0.019(95% CI: 0.92, 0.96). Similarly, it was 91.0% 0.015(95%CI: 0.87, 0.93) and 86.9% 0.01 (95%CI: 0.82, 0.90) at the end of second and third days respectively.

The overall mean and median survival time of low-birth-weight neonate admitted to NICU in the study was 18 and 22 days respectively. At the 7th days of hospital stay the probability of survival of low-birth-weight neonate was found to be 71.47% with a standard error of 0.027 (95%CI:0.65,0.76), at 14th from days of hospital stay the probability of survival of low-birth-weight neonates was 59.38 % with a standard error of 0.036 (95%CI:0.52, 0.61) and the over all probability of survival of low-birth-weight neonate was 47.31% with a standard error of 0.05 (95%CI:0.39,0.56) for the follow up period of time (Figure 1).

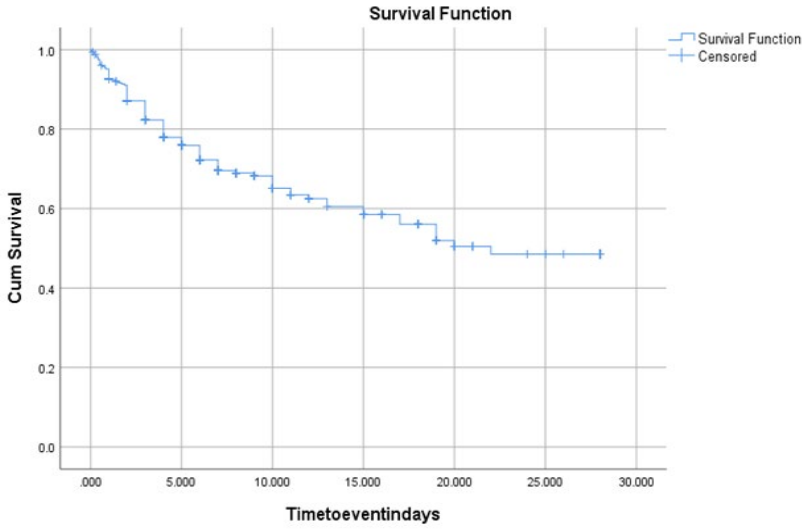

Figure 1: The Overall Kaplan-Meier Estimates Among Neonates Admitted With Low-Birth-Weight At Governmental Hospitals Addis Ababa, Ethiopia, 2021.

- The log rank estimate of mortality among the covariates of the variables

Log-rank test was conducted to check for the existence of any significant differences in survival among various levels of the categorical predictors considered in the study. Accordingly, the Kaplan-Meier analysis indicated significant evidence of differences in survival times in the categories. Based on this statistical test mode of delivery, cry immediately after birth, resuscitation done immediately after birth, first and fifth minute APGAR score, neonates kept in kangaroo mother care, type of feeding within the first 28 days of life, prematurity, birth-weight, apnea, asphyxia, respiratory distress, prematurity, NEC, disseminated intravascular coagulopathy and use of CPAP are statistically significant (P-value<0.05). This means that, we have enough evidence to say low-birth-weight neonates admitted to NICU survival curves were different or the Kaplan Meier curves are statistically different with respect to categories (Table 3).

Variables	Category	Survival		Log-rank test	P-value
		Mean (95% CI)	Median(95%CI)		
Residency	Urban	17.5(15.8, 19.2)	20.00	0.305	0.55
	Rural	18.8(15.1, 22.4)	22.00		
Sex of neonate	Male	17.2(15.1, 19.2)	19.0(13.5,25.5)	0.356	0.58
	Female	18.6(16.3, 20.9)			
ANC visit	Yes	17.9(16.4, 19.5)	22.00	0.72	0.39
	No	9.0(5.1, 12.9)	7.00(1.0, 12.9)		
Birth weight	<1000gram	6.3(3.2, 9.3)	3.00(2.2, 3.7)	69.53	0.000
	1000-15000gram	16.6(14.2, 18.9)	19.00		
	1500-2500gram	20.9(18.7, 23.1)			
Cry immediately after birth	Yes	19.1 (17.3, 20.9)		17.99	0.000
	No	12.8 (9.5, 16.2)	6.0(0.7, 11.3)		
	Unknown	12.3 (5.6, 19.1)	6.0(2.1, 9.9)		
Resuscitation at birth	Yes	12.8 (9.4, 16.3)	7.0(0.0, 14.4)	14.64	0.000
	No	18.7 (17.0, 20.4)			
1st minute APGAR score	<7	17.0(15.2, 18.8)	19.0(13.5, 24.9)	6.95	0.000
	>7	22.5(19.2, 25.8)			
5th minute APGAR score	<7	15.2(12.8, 17.7)	6.4(4.4, 29.6)	14.29	0.000
	>7	19.3(17.3, 21.5)			
Apnea	Yes	7.3 (4.9, 9.5)	3.0(1.0, 4.1)	103.76	0.000
	No	21.0(19.4, 22.7)			
EONS	Yes	19.2(16.4, 21.9)	19.0	1.04	0.309
	No	17.2(15.4, 19.0)			
Asphyxia	Yes	13.3(10.2, 16.5)	7.0	14	0.000
	No	18.7(16.9, 20.5)			
DIC	Yes	9.1 (3.1, 15.1)	4.0(0.9, 7.1)	7.03	0.000
	No	18.1 (16.5, 19.7)			
NEC	Yes	12.7(9.0, 16.3)	7.0(4.5, 9.5)	7.14	0.000
	No	18.8(17.2, 20.4)			
RD	Yes	16.2(14.4, 18.0)	19.0(12.5, 25.5)	13.28	0.000
	No	20.8(17.8,23.84)			
Prematurity	Yes	16.9(15.1, 18.7)	19.0	4.82	0.000
	No	20.5(17.4, 23.6)			
Only EBM feeding in hospital stay	Yes	21.6(20.0, 23.0)	2.0(1.5, 2.5)	199.40	0.000
	No	4.4 (3.2, 5.5)			
Kept in KMC	Yes	27.2(25.8, 28.7)	19.0(12.9, 25.1)	13.73	0.000
	No	16.6(14.9, 18.3)			
CPAP	Yes	22.3(19.9, 24.6)		39.89	0.000
	No	14.0(12.0, 15.9)	10.0(2.6, 17.3)		

Table 3: The Kaplan Meier Estimates of Mean Survival Time for the Covariates Among Low-Birth-Weight Newborns Admitted at Neonatal Intensive Care Units in Governmental Hospitals of Addis Ababa, Ethiopia,2021.

- Survival function and Comparison of Survivorship Functions for different categorical variables

The Kaplan-Meier estimator survival curve gives an estimate of survival function among different groups of covariates to make comparisons. Separate graphs of the estimates of the Kaplan-Meier survivor functions were constructed. Survival function lying above another means the group defined by the upper curve has a better survival than the group defined by the lower curve or had a more favorable survival experience than the group defined by the lower curve. For example, neonates who feed only EBM within follow-up time had higher survival time (22 days (95% CI: 20, 23) as compared to their counterparts those feed additional formula milks 4days (95%CI: 3, 6) this difference was statistically significant with p value = 0.000 (Figure 2).

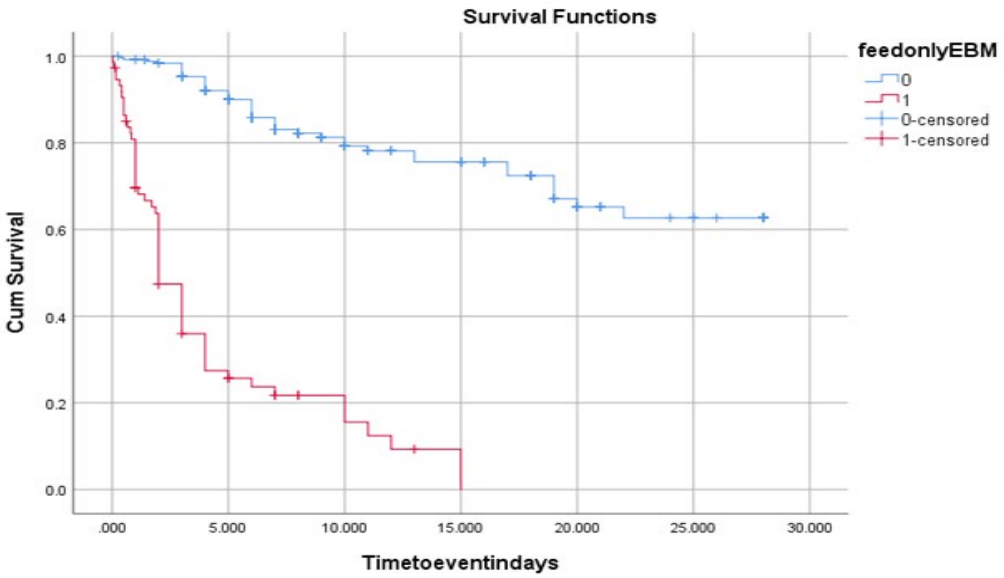

Figure 2: The Kaplan-Meier Survival Curves Compare Survival Time Of Neonates Admitted With Low-Birth-Weight For Variable Feed Only Ebm At Governmental Hospitals Of Addis Ababa, Ethiopia,2021.

Another example on low-birth-weight neonates with asphyxia shows that there is a significant survival time difference in the category. The median survival time for low-birth-weight neonates who developed asphyxia was 13 days (95% CI: 10.20, 16.50), but it was longer 19 days (95%: 16.97, 20.52) days for neonates who does not develop asphyxia the difference was significant (p-value<0.001) Figure (3).

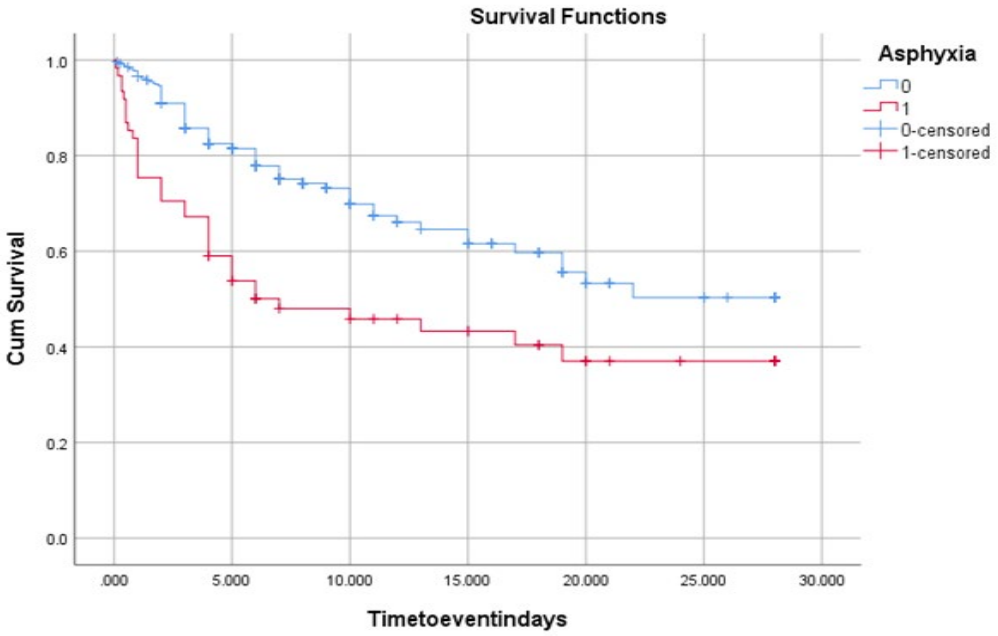

Figure 3: The Kaplan-Meier Survival Curves Compare Survival Time Of Neonates Admitted With Low-Birth-Weight For Variable Asphyxia At Governmental Hospitals Of Addis Ababa, Ethiopia, 2021.

7.7 Predictors of Mortality among Low-Birth-Weight Newborns

The relationship between the baseline variables and the hazard of mortality was analyzed using Cox proportional hazard regression model. The Cox proportional hazard model in Table 4 shows that maternal factors like mode of delivery, gestational age, birth-weight, first minute APGAR score, fifth minute APGAR score, resuscitation after birth, cry after birth, apnea, preterm, DIC, NEC, RDS, asphyxia, CPAP kangaroo mother care and EBM feeding were statistically significant (p-value < 0.05) predictors of low-birth-weight neonatal mortality in bi-variable cox proportional regression analysis. Moreover, to identify independent predictors of time to death multivariable cox regression was performed for all predictors found to be significantly predicted with survival in the bivariate analysis (Table 4).

Variables	Categories	Total	CHR (95% CI)	AHR (95% CI)
Mode of delivery	SVD	196	1.58(1.04, 2.38)	1.41(0.88, 2.26)
	Instrumental	3	0.000(0.0000, 5.01+177)	0.0000(0.0000, 1.1E+266)
	C/S	130	1	1
Cry immediately after birth	No	53	2.32(1.51, 3.56)	1.02(0.34, 3.01)
	Unknown	17	2.10(1.10, 4.39)	0.91(0.11, 7.32)
	Yes	258	1	1
Resuscitated immediately after birth	Yes	51	2.22(1.45, 3.39)	0.83(0.29, 2.35)
	No	278	1	1
First minute APGAR score	<7	250	0.41(0.21, 0.82)	1.02(0.34, 3.01)
	>7	57	1	1
Fifth minute APGAR score	<7	116	0.47(0.32,0.71)	1.01(0.56, 1.82)
	>7	196	1	1
Birth weight	<1000gm	31	7.06(4.19, 11.87)	2.14(1.06, 4.30) *
	1000-1500gm	1112	2.15(1.37, 3.38)	1.66(0.95, 2.89)
	1500-2500gm	186	1	1
Kept in KMC	Yes	26	1	1
	No	303	15.54(2.16, 111.75)	8.86(1.15, 68.52) *
Only EBM feeding during follow-up time	Yes	255	1	1
	No	74	11.00(7.27, 16.65)	8.74(5.26-14.57) *
Apnea	Yes	64	5.71(3.89, 8.39)	3.04(1.87, 4.94) *
	No	265	1	1
Asphyxia	Yes	61	2.12(1.41, 3.20)	2.34(1.04, 5.26) *
	No	268	1	1
Respiratory distress	Yes	212	2.46(1.48, 4.08)	1.24(0.65, 2.37)
	No	117	1	1
Prematurity	Yes	233	1.72(1.05, 2.83)	0.92(0.47, 1.79)
	No	96	1	1
DIC	Yes	10	2.53(1.23, 5.21)	1.02(0.39, 2.63)
	No	319	1	1
NEC	Yes	28	1.91(1.17, 3.11)	0.68(0.37, 1.21)
	No	301	1	1
CPAP	No	156	4.10(2.54, 6.63)	1.25(0.59,2.64)
	Yes	173	1	1

Table 4: Predictors of Mortality among Newborns with Low Birth Weight in Neonatal Intensive Care Units of Governmental Hospitals in Addis Ababa, 2021.

*Variables which have P-value <0.05 in multivariable logistic regression analysis

CHRs reflect bivariate modeling results, whereas AHRs are taken from a multivariate model containing all variables in the table and categories labeled as 1 are considered as reference categories.

The results of multi-variable analysis shown that low-birth-weight neonates who have birth weight less than 1000gram have two times higher hazard of mortality than those who have birth weight between 1500gm to 2500gram (AHR: 2.14; 95%CI: 1.06, 4.30). Newborns that develop apnea during follow-up time have three times higher hazard of mortality than their counterparts (AHR: 3.04; 95%CI: 1.87, 4.94). The hazard of mortality among asphyxiated newborns was three times higher than those who didn't asphyxiate (AHR: 2.34; 95%CI: 1.04, 5.26). The hazard of mortality among newborns with low birth weight who didn't feed only exclusive breast-feeding during follow-up time was nine times higher than their those who have feed only exclusive breast milk (AHR: 8.74; 95%CI: (5.26-14.57). Low-birth-weight newborns who didn't kept under KMC have nine times higher risk of mortality than those their counterparts (AHR: 8.86; 95%CI: 1.15, 68.52) (Table 4).

8. Discussion

In this retrospective follow up study, we aimed to determine the survival status and predictor of mortality among low-birth-weight neonate admitted to NICU of selected Addis Ababa governmental hospitals, 2021. This study shows that the overall mortality of low-birth-weight neonates admitted to NICU during the study period was 31.9%. This finding is higher than the study done in Arba Minch (8.3%)(9) and lower than a study conducted at Central Hospital in Johannesburg (74.49%) (18). This gap might be due to different reasons. One possible source of variation in mortality rate might be difference in sample size. Further, possible reasons might be the difference in methodology. Other, possible justification might be the difference in the study period as there were changes in treatment modality. At the end of follow up, the overall incidence of mortality was found to be 40.2 deaths per 1000 person-day observation. This finding is higher than a study conducted at Arba Minch which founds the incidence of mortality among low-birth-weight was 14.5 per 1000 neonate days (person time of observation) [9]. This difference might be due to the difference between the study populations. The study population of our study are critical neonates referred from different parts of Ethiopia because the study are main referral centers of patients from private hospitals, governmental hospitals, from health centers of Addis Ababa and also from different parts of Ethiopia. The overall mean survival time of low-birth-weight neonate admitted to NICU in the study was found to be almost 17.76 days which is consistence with a study in Ethiopia, the overall mean survival time and median survival time was 17.13 days [9].

After adjusted by multi-variable cox proportional regression model, the independent significant predictors for time to death were EVLBW, KMC, EBM feeding, asphyxia and apnea. In this study, the hazards of mortality among low-birth-weight newborns with asphyxia were two times higher than their counter parts (AHR: 2.34: 95%CI: 1.04, 5.26). This finding is consistent with the study conducted in Tigray(8). The probable explanation for this might be because of the complications of asphyxia. Asphyxiated newborns have higher probability to develop problem in the main body organ systems like renal, brain, respiratory system, gastro-intestinal system and others.

Newborns with low-birth-weight who develop apnea during follow-up time have four times higher hazard of mortality than their counterparts or those not apneic during follow up time (AHR: 4.22,95%CI; 1.76, 10.12). This might be because apnea can cause respiratory failure. Being EVLB neonates increases the hazard of time to death by more than two folds compared with those neonates having birth-weight between LBW neonates (AHR: 2.31, 95%CI; 0.98, 5.41). This finding is nearly similar with study done in England, which shows neonatal mortality rates were significantly greater in the VLBW [7]. This might be due to the complications related to the immaturity of different organs like respiratory system, cardiovascular system, gastro intestinal system, immunity for host defense and others because birth weight is proportionally related to gestational age of the new born [19,20]. Similar with the study conducted at neonatal intensive care units of Arbaminch general hospital, in Ethiopia, newborns with low birth weight who did not kept under kangaroo mother care within one hour of delivery had nine times higher hazard of mortality as compared with the counterparts who were kept under kangaroo mother care within one hour (AHR: 8.86; 95%CI: 1.15, 68.52) [9]. This might be due to kangaroo mother care enhances early and continuous skin to-skin contact between mother and baby as well as promotes exclusive breastfeeding which is recommended by WHO [21]. A Johannesburg study shows that kangaroo mother care results in a forty-eight percent relative reduction in mortality among low-birth-weight newborns. A Cochrane neonatal review conducted to assess the benefit and adverse effects kangaroo mother care shows that KMC was associated with a statistically significant reduction in risk of mortality at discharge or at 40 to 41 weeks' postmenstrual age [18,22].

The hazard of mortality among newborns with low birth weight who didn't feed only exclusive breast feed within one hour was nine times higher as compared with their counterparts (AHR: 8.74; 95%CI: 5.26-14.57). This finding is consistent with the study conducted at Arbaminch, Ethiopia [9]. This could be because early initiation of exclusive breast-feeding enables the newborn to receive the colostrum or which has full of protective factors [23].

Preterm birth, maternal history of diabetes mellitus and HIV, lack ANC follow up, previous history of small baby and mode delivery were declared as statistically significant in previous studies but they are not statistically significant in this study [16,18,20,24]. Therefore, meta-analysis study might be required.

9. Strength and Limitations of the Study

Being used cohort study design and multicenter institutions

were among the main strength of this study whereas, being used retrospective or chart review was the limitation of this study.

10. Conclusion

In the current study, 105 (31.9%) neonates were died during the follow up period. Hence, the overall incidence rate was 40.2 per 1000-person day; the overall mean and median of time to death were 18 and 22 days respectively. The survival status of the neonates admitted with low-birth-weight was lowest at the early admission period especially at the first week and gradually decreases at the later follow up weeks. Lack of kangaroo mother care, unable to feed only EBM feeding, birth weight less than 1000gram, neonates who have concurrent problems of asphyxia and apnea were statistically significant predictors of time to death.

Declarations

Ethical Approval and Consent to Participate

An approval of the proposal was obtained from the research and ethics committee Department of Nursing and Midwifery, Addis Ababa University (AAU). After the approval of the proposal the letter was submitted to TASH and Addis Ababa health bureau (AAHB). Ethical clearance was obtained from Addis Ababa public health research and emergency management directorate. The collected data was kept confidential and no one except the members of the research team has access to it. All paper of the study was kept in a secured place &the name or other personal information has not been notified in any report. The data collection was started after official permission was secured from selected four hospitals to conduct the study and to assess the record.

Consent for Publication

All authors approved that this manuscript is eligible for publication.

Availability of Data and Materials

The data and other documents used in this study are available from the corresponding author.

Competing Interests

The authors declare that they have no conflict of interest.

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Authors' contributions

DB and JG: conceptualization, methodology, software, formal analysis, writing original draft. NM and FB: validation, methodology, reviewing & editing. Finally, all authors approved the manuscript.

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