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Journal of Pediatrics & Neonatal Care

Research Article

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Time to death and its predictors among early neonatal patients in neonatal intensive care unit of Dessie referral hospital, South Wollo Zone, Northeast Ethiopia

Abstract

Background: Early neonatal death is a serious concern, both in the developing and developed worlds. Early neonatal death remains a health problem and is the biggest component of the neonatal mortality rate. Therefore, substantial reduction in early neonatal mortality is a crucial pre-requisite for achieving further gains in child survival in the country. However, the distribution of deaths in the community within the first week is poorly understood. Therefore, this study was conducted to assess time to death and its predictors among early neonates in the neonatal intensive care unit of Dessie Referral Hospital.

Method: A retrospective cohort study was conducted in the early neonatal patient in Dessie referral hospital on the total sample size of 416 selected patients by using a simple random sampling technique. Data were collected by document review. Life table used to estimate the probability of survival, log-rank test to compare survival in two or more groups and the Cox proportional hazard model was used to determine factors associated with time to death of early neonate. The hazard ratio with 95% confidence level was used to declare statistical significant association.

Result: A total of 416 early neonates were included in the study. There were 224(53.8%) male neonates. The overall early neonatal mortalities were 47(11.3%), of which 23.41% of them died on the first day of age. early neonatal mortality was associated with neonatal sepsis (AHR=3.349,95% CI,1.842-6.089), low birth weight of neonates (AHR=3.563%,95% CI,1.925-6.595), unable to breastfeeding during delivery (AHR=4.094,95% CI,1.603-10.452), neonatal respiratory distress (AHR=4.018,95% CI,1.733-9.371), perinatal asphyxia (AHR =2.540,95% CI,1.186-5.847).

Conclusion: The causes of early neonatal death described in this study were preventable. Managing low birth weight, initiating exclusive breastfeeding, refining quality of service, and confirming the continuity of care are recommended to increase the survival of neonates.

Keywords: time to death, early neonatal, predictors, nicu

Volume 12 Issue 3 - 2022

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Received: August 18, 2022 | **Published:** September 10, 2022

Abbreviations: NICU, neonatal intensive care unit; ENM, early neonatal mortality; HEP, health care provider

Background

The early neonatal period could be a profoundly vulnerable time for a newborn child completing numerous of the physiological alterations required for life exterior of the uterus. As a result, there is a high rate of morbidity and mortality.[1] Early neonatal death is defined as all death of a live-born infant on or before the first seven days of life.[2] About two-thirds of infant deaths occur in the neonatal period, of which nearly two-thirds die during the first week, and of these two-thirds die during the first 24 hours.[3,4]

Early neonatal death accounts for 75% of all neonatal deaths worldwide.[5] Globally, 2.4 million children died in the first month of life in 2019, with approximately 6,700 neonatal deaths every day, most of which close to three quarters dying in the first week, with one-third dying on the first day.[6] Over the past decades, mortality during the early neonatal period declined more slowly than late neonatal and post neonatal infant mortality.[7] All inclusive, stamped incongruities in neonatal mortality exist over districts and nations. Across the globe, neonatal mortality rates range from 5 per 1000 in developed countries to 50 per 1000 in the least developed countries.[8] Sub-Saharan Africa is by far the risk region to be born. In sub-Saharan Africa, babies are more than 7 times as likely to die on the day they are born as babies in industrialized countries.[9]

In 2015, the Joined together Countries summit on maintainable improvement formally received the 2030 plan for maintainable advancement. In the Sustainable Development Goals, the goal is to end preventable neonatal and under-five child deaths by 2030, with all nations pointing to decrease neonatal mortality to at slightest as moo as 12 deaths per 1000 live births and under-five mortality to at slightest as moo as 25 deaths per 1000 live births.[10] However, Sub-Saharan Africa is the only SDG region to see no decline in the number of neonatal deaths from 1990 to 2019.[6]

Early neonatal survival is the most important indicator of improving health care during childbirth and the life quality of a given population.[11] There are various factors that may be associated with early neonatal mortality and they have been the reasons for the wide variation in mortality rates among the health facilities reporting. One of the three major causes of ENM is intrapartum-related neonatal death, especially birth asphyxia[12,13]. Another significant risk factor is preterm birth, which leads to small size at birth, or a timely delivery

but that the child is small-for-gestational-age[12,14] often caused by malnutrition of the mother.[15] Small size at birth is correlated to neonate hypothermia and infections, which both increase the risk of the neonate dying during the ENM period.[16] The third major cause of ENM is severe infections, where sepsis and pneumonia are the two major killers, but tetanus and diarrhea are also important causes.[12,13]

Ethiopia is one of the sub-Saharan countries that have a high neonatal mortality rate, and even one of the top ten countries in Africa.[17] To reduce neonatal deaths, the Ethiopian government has implemented many health interventions such as training midwives, enhancing the referral system, integrating health services, implementing packages of the Health Extension Program (HEP), and routine immunization.[18] In spite of many efforts by the government and other stakeholders, a non-significant and very sluggish decline has been achieved. Distinguishing the determinants and causes of early neonatal mortality at the nearby setting may be an exceptionally vital and convenient issue. Past literature on the subject matter has continued to give more emphasis to either under-five mortality[19–21] or neonatal mortality[22–24] ignoring the significant proportion of early neonatal deaths as a critical component of both neonatal and under-five mortalities.

Therefore, understanding early neonatal mortality in connection to these factors is pivotal. This is because there are highly feasible and cost-effective interventions that could avert this mortality, and this can only be achieved if countries adopt locally relevant and focused interventions that are guided by evidence. So this study was interested in dealing with an estimate of the survival rate in addition to identifying primary etiological factors responsible for early neonatal mortality and the relative contribution of these factors to early neonatal mortality. So the result of this study provides a crucial data of survival and predictors of survival of neonate to the health care provider, at a different level, so that it will allow for closer follow up of high-risk patients and more targeted interventions will be made that reduces mortality and improve quality of life of patients.

Methods and Material

Study design, setting and period

A retrospective follow up study was conducted in the Dessie referral hospital of Dessie town, Amhara Regional State, Ethiopia from January 4, 2017, to January 6, 2020.

Population

The source population was all early neonates who were admitted to the Dessie referral hospital intensive care unit, and the study population was all early neonates who were admitted to Dessie Referral Hospital from January 4, 2017-January 6, 2020.

Inclusion and exclusion criteria

All early neonates who were admitted to the neonatal intensive care unit in Dessie referral hospital were included, and early neonates with incomplete data were excluded.

Sample size determination and sampling procedures

The total sample size was determined by Epi info version 7.2, which included 416 early neonates. Based on the assumptions from the previous study of 2.03 hazard-ratios, 10% outcome in an unexposed group with a gestational age of neonate.[25] There was an accepted error of 5%, power of 80%, and 95% confidence level.

All the study participants who were found in neonatal registration logbooks of the past three years (January 4, 2017 – January 6, 2020) were checked for chart retrieval. After that, a chart that had accessed was taken for sampling by using computer-generated random numbers was used to select the predetermined required sample size. Charts with incomplete data were excluded, and the next random number was taken.

Study variable

Time to death of early neonates was the dependent variable and the independent variable included neonatal characteristics and maternal characteristics.

Data collection tools and Quality control

Data were collected by using a checklist developed based on the maternal card, neonatal card, and neonatal patient registration logbook which is adopted by the federal minister of health. Its quality was controlled by designing proper data collection tools, pre-testing, and continuous supervision and before actual data collection, training was provided to BSC nurse data collectors for two days on the data collection techniques to familiarize data collectors with the tool. Data were collected by reviewing maternal cards, neonatal cards, and a neonatal registration log book.

Data processing and analysis

Data were entered in Epi data 3.1 and it was checked, cleaned, and edited before analysis, and it was exported to SPSS version 23 for analysis. Describe the patient cohort characteristics in terms of the mean value for continuous data and percentage for categorical data. The survival time was calculated in a day using the time interval between the date of birth and the end of the follow-up period. A life table was applied to estimate the probability of the survival of the patient and a log-rank test was used to compare the KM curve for two or more categories of patients. The multivariable Cox proportional hazard model was used to determine the relationship between the independent variable and the outcome variable. The Cox proportional hazard assumption was checked graphically. The first bivariable analysis was made for each independent variable to the outcome variable, and those variables resulting p-value less than 0.3 was entered to the multivariable Cox regression model. In the final model, those variables with a p-value less than 0.05 were considered as statistically significant, and it was presented by hazard ratio (HR), with a 95% confidence level (CI) to show the strength and direction of the association.

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board (IRB) of Wollo University, College of medicine, and health science. Following the approval by the IRB, the official letter of co-operation was written to the concerned bodies by Wollo University. As the study was conducted through a review of medical records, the individual patients were not subjected to any harm as far as confidentiality is kept. To preserve confidentiality, no personal identifier was used on the data collection form, and the recorded data was not accessed by a third person except the principal investigator.

Result

Data were collected from all 416 study participants born between January 4, 2017 and January 6, 2020.

Neonatal characteristics

The mean age of the neonates was found to be 3.62 days (SD=±4.4). Among the cohort, 224 (53.8%) were male. Of these (416) neonates,

20.9% of them had neonatal sepsis, 17.1% had respiratory distress syndrome and 15.1% had perinatal asphyxia. Regarding birth weight, 65.1% of them had a normal birth weight (2.5-4 kg). With respect to their anthropometrics, more than three-fourth of (91.5%) neonates had the appropriate size for gestational age (Table 1).

Maternal characteristics

The mean age of mothers during delivery was 26.95 years (SD=±4.4). Among the total number of mothers recruited for the study, 98.3% had received two doses of the TT vaccine, 98.6% had breastfed during delivery, 1.7% had a history of stillbirth, and 1% had a history of abortion (Table 2).

Table 1 Neonatal characteristics of early neonate admitted to NICU in Dessie referral hospital in 2020

Neonatal characteristics	Categories	Total Frequency (%)	Death Frequency (%)
Age	1 day	27(6.49%)	11(23.41%)
	2-7 day	389(93.51%)	36(76.59%)
Sex	Male	224(53.84%)	29(61.7%)
	female	192(46.15%)	18(38.29%)
neonatal sepsis	yes	95(22.8)	29(61.7%)
	no	321(77.2%)	18(38.29%)
neonatal Apgar score 1 minute	3-Jan	8(1.9%)	2(4.25%)
	10-Jul	223(53.6%)	28(59.59%)
	6-Apr	185(44.47%)	17(36.17%)
neonatal Apgar score 5 minute	<=6	66(15.86%)	16(34.04%)
	10-Jul	350(84.13%)	31(65.95%)
neonatal birth weight	< 2.5 KG	138(33.17%)	31(65.95%)
	2.5-4 KG	271(65.14%)	16(34.04%)
	>4KG	7(1.68%)	0
neonatal jaundice at admission	yes	9(2.16%)	1(2.1%)
	no	407(97.83%)	46(97.89%)
neonatal congenital abnormality	yes	5(1.2%)	0
	no	411(98.79%)	47(100%)
neonatal respiratory distress syndrome	yes	71(17.1%)	32(68.08%)
	no	345(82.9%)	15(31.92%)
perinatal asphyxia develop	yes	63(15.14%)	28(59.57%)
	no	353((84.85%)	19(40.42%)
size for gestational age	appropriate for gestational age	381(91.58%)	39(82.9%)
	small for gestational age	28(6.73%)	8(17.02%)
	large for gestational age	7(1.68%)	0
Temperature	<36.5	272(65.38%)	40(85.1%)
	36.5-37.5	131(31.49%)	6(12.76%)
	>37.5	13(3.12%)	1(2.12%)
gestational age	<37 week	96(23.07%)	25(53.19%)
	37-42week	319(76.68%)	22(46.8%)
	>42week	1(0.24%%)	0

Table 2 Maternal factors of early neonate admitted to NICU in Dessie referral hospital in 2020

Maternal characteristics	Categories	Total frequency (%)	Death frequency (%)
Maternal age in year	<20	10(2.4%)	3(6.4%)
	20-30	346(83.17%)	37(78.7%)
	>30	60(14.42%)	7(14.9%)
Mother take TT vaccine	= <2 doses	409(98.3%)	46(97.9%)
	>2 doses	7(1.7%)	1(2.1%)
HIV status of the mother	Positive	4(1%)	1(2.1%)
	negative	412(99%)	46(97.9%)
VDRL result of the mother	positive	1(0.2%)	0
	negative	415(99.8%)	47(100%)
Breast feed of the mother during delivery(<1hr)	yes	410(98.6%)	42(89.4%)
	no	6(1.4%)	5(10.6%)
History of still birth	yes	7(1.7%)	1(2.1%)
	no	409(98.3%)	46(97.9%)
History of abortion	yes	4(1%)	2(4.25%)
	no	412(99%)	45(95.75%)
Parity of the mother	prime	76(18.3%)	9(19.2%)
	44565	322(77.3%)	33(70.2%)
	>4	18(4.3%)	5(10.6%)

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Table Continued...

Maternal characteristics	Categories	Total frequency (%)	Death frequency (%)
Mothers type of gestation	singleton	387(93%)	42(89.4%)
	multiple	29(7%)	5(10.6%)
Mode of delivery of mother	cesarean section	112(27%)	12(25.5%)
	spontaneous delivery	285(68.5%)	35(74.5%)
	instrumental delivery	19(4.5%)	0
ANC follow up	4 times	390(93.75%)	45(95.7%)
	<4 times	26(6.25%)	2(4.3%)
Pregnancy related Complication	No complication	328(78.8%)	32(68.1%)
	Eclampsia(preeclampsia)	33(8%)	5(10.64%)
	Prom	25(6%)	5(10.64%)
	Anemia	15(3.6%)	4(8.5%)
	Diabetes mellitus	15(3.6%)	1(2.12%)

Follow up outcome

All the study subjects were followed for seven consecutive days, but for different reasons participants were retained in the cohort for different lengths of time, they stay for a minimum of one, a maximum of seven days, and the median time was unreached (Figure 1). From a total of 416 cases, 22(5.3%) of them were referred to higher health facilities, and the remaining 11(2.6%) of them were against the treatment.

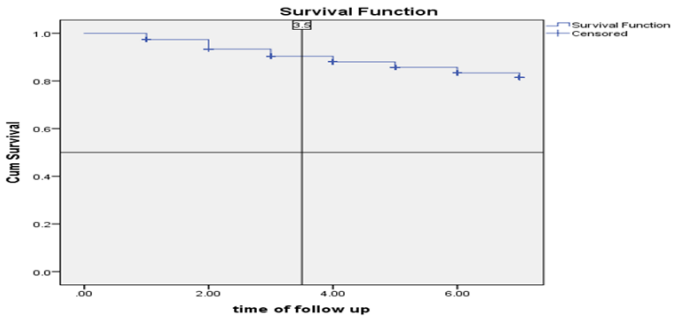

Figure 1 The median survival time for early neonate in Dessie Referral hospital NICU in 2020.

Survival

As it's mentioned before, the study subjects were stayed for different lengths of time in the cohort making the general population at risk of 1508 person day follow up. The total of death in the study period was 47 this makes the instantaneous hazard rate 47/1508=9.3 per day per 1000 Neonates. In this study, 23.4% of the death occurred on the first day, and 76.6% of death occurred between 2-7 days. As per the analysis of the data from all study participants (416) the cumulative probability at 1 and 7 days is 97% and 77% respectively (Table 3).

Predictors of Early neonatal mortality

The relation between the main variable and the risk of death was analyzed using the bivariable Cox proportional hazard model. Only a total of 383 neonates who had different lengths of follow-up were included in bivariable and multivariable Cox regression analysis by excluding those transferred and against patients.

In the final multivariable Cox regression analysis, Neonatal sepsis (P<0.001), neonatal birth weight (p<0.001), neonatal respiratory distress syndrome (p=0.001), Perinatal asphyxia (p=0.021), and mother's breastfeeding during delivery (p=0.003) remain in the final model as statistical significant predictor with the timing of early neonatal mortality (Table 4).

Table 3 Life table estimates of the cumulative progression to death for 416 cohorts admitted to NICU for seven days between January 4,2017 up to January 6,2020

Interval start time	Number entering interval	Number withdrawing during interval	Number of terminal event	Proportion surviving	Commutative proportion surviving at the end of interval	Hazard rate
1	416	16	11	0.97	0.97	0.03
2	389	93	16	0.95	0.93	0.05
3	280	80	9	0 .96	0.89	0.04
4	191	70	5	0 .97	0.86	0.03
5	116	40	3	0 .97	0.84	0.03
6	73	28	2	0 .97	0.81	0.03
7	43	42	1	0 .95	0.77	0

Table 4 The bivariable and Multivariable cox-regression analysis of the death outcome among the early neonates in Dessie Referral Hospital NICU, 2020

Variable	Categories	Death	Censored	CHR	AHR	95% CI
Neonatal sepsis	Yes	29	55	8.231	3.349	(1.842 -6.089)^{xxx}
	No	18	281	1		1
Neonatal birth weight during delivery	<2.5kg	31	101	4.508	3.563	(1.925 - 6.595)^{xxx}
	>=2.5kg	16	235	1		1
Neonatal respiratory distress syndrome	Yes	32	36	17.778	4.018	(1.733 - 9.317)^{xx}
	No	15	300	1		1

Table Continued...

Variable	Categories	Death	Censored	CHR	AHR	95% CI
Perinatal asphyxia	Yes	28	35	12.674	2.54	(1.186 - 5.847)^{xx}
	No	19	301	1		1
Breast feeding during delivery(<1hr)	Yes	42	335	1		1
	No	5	1	39.881	4.094	(1.603 - 10.452)^{xx}
neonatal Apgar score 5 minute	<=6	16	50	3.293	1.646	(0.872 – 3.108) ^{x}
	10-Jul	31	319	1		1
size for gestational age	Appropriate for gestational age	39	349	1		1
	Small for gestational age.	8	20	3.508	2.416	(0.989 – 5.902) ^{x}
gestational age	<37 week	25	71	1		1
	>=37week	22	298	4.77	1.735	(0.753 – 3.998) ^{x}

x= p-value > 0.05 xx = p-value =< 0.05 xxx = p- value < 0.01

Hazard Function of the Predictor Variables

Neonatal sepsis had a significant association with the timing of early neonatal mortality, with statistical significant difference among the categories. (diseased vs non diseased) (Log-rank test, p value <0.001) (Figure 2).

Perinatal asphyxia was the other determinant factors which had a significant association with the timing of early neonatal mortality with statistical significant difference among categories (diseased vs non diseased)(log-rank test, p value <0.001) (Figure 3).

The birth weight of the neonate was the other determinate factor which had a significant association with the timing of early neonatal mortality with statistical significant difference among different categories. (>=2.5kg vs<2.5kg) (log-rank test, p value <0.001) (Figure 4).

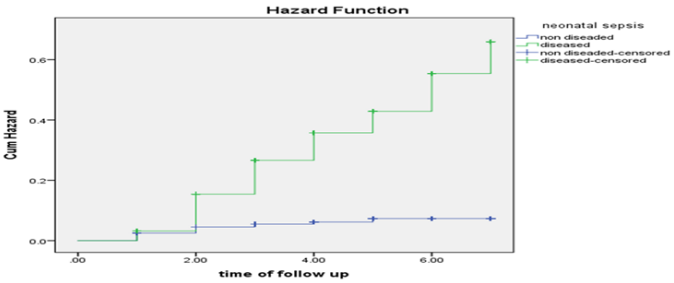

Figure 2 Hazard plot of neonatal sepsis among different categories of early neonate, 2020.

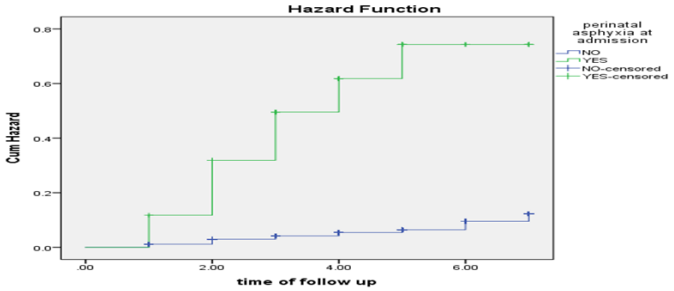

Figure 3 Hazard plot of perinatal asphyxia among different categories of early neonate, 2020.

The other categories of predictor were which had an association with the timing of early neonatal mortality was breastfeeding of a mother during delivery, there was a statistical significance difference among categories (breastfeed vs non breastfeed) (log-rank test value <0.001) (Figure 5).

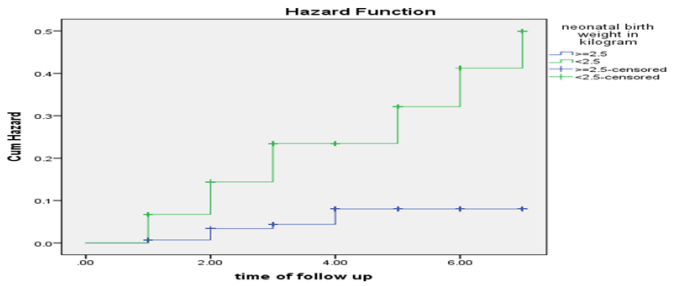

Figure 4 Hazard plot of birth weight among different categories of early neonate, 2020.

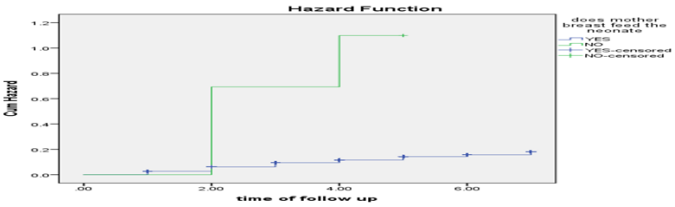

Figure 5 Hazard plot of breast feeding during delivery among categories of early neonatal, 2020.

The other categories of predictor were neonatal respiratory distress syndrome which has an association with the timing of early neonatal mortality with the statistical difference among categories (diseased vs non diseased) (log- rank test value <0.001) (Figure 6).

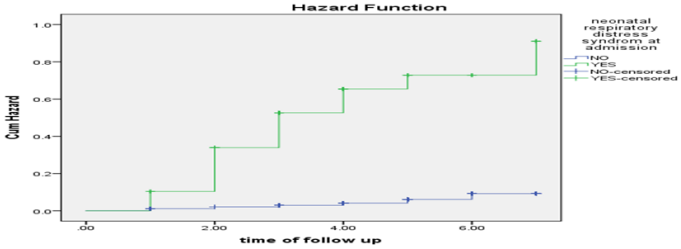

Figure 6 Hazard plot of neonatal respiratory syndrome among categories of early neonatal, 2020.

Discussion

In this study, the early neonatal mortality proportion was 11.3% with 95%CI (8.4-14.7). This proportion was lower when to compare with the study done in Black Lion specialized hospital. 26 This difference might be due to the complicated cases that were referred to Black Lion Hospital. But Dessie referral hospital NICU mortality proportion was comparable with the study done in Gondar and Bahir Dar.[27,28]

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However, it was higher than a study conducted in southwest Ethiopia.[29] These variations might be due to methodological differences among studies and dissimilarities in socio-cultural, health service utilization, and economical variations among study participants.

The median survival time of the study participants was found to be unreached. Which was similar to the study finding in Tigray Ethiopia.[30] But the median survival time was reached in a different place like North West Ethiopia.[31] This difference might be due to the short follow- up period and a higher number of right-censored cases.

In accordance with this study finding, the neonates who develop neonatal sepsis had a commutative hazard was found to be 3.34 times at high risk of death when compared to those who do not develop neonatal sepsis. The relationship between neonatal sepsis and mortality among neonates was also shown in similar studies done in Gondar and Eritrea.[27,32] Being infected with neonatal sepsis indicates that the neonates cannot suck, and the neonate had vomiting, diarrhea, poor perfusion, and hypothermia, which are associated with increased risk of mortality.

Neonates with low birth weight had a commutative hazard was found to be 3.56 times high risk of death when compared to those who had normal birth weight. The association observed between low birth weight and mortality in this study was similar to previous studies done in Addis Ababa, South West Ethiopia, Eretria, and Egypt.[26,29,32,33] Low birth weight indicators of poor intrauterine growth and low birth weight of neonates were at high risk of a motor, cognitive, behavioral, and emotional problem, which leads to mortality.

Those neonates who develop respiratory distress syndrome had a commutative hazard was found to be 4 times the high risk of death when compared to those who do not develop respiratory distress syndrome. This finding was supported by a study done in South West Ethiopia and Egypt[(29,33)]. Various studies showed this respiratory distress syndrome related to preterm, poor prenatal care, and low maternal body mass index which increased the risk of mortality of neonates.[34,35]

Neonates who developed neonatal asphyxia had a commutative hazard was found to be 2.54 times the high risk for early neonatal mortality than those who did not develop neonatal asphyxia. This finding is also supported by studies done in Addis Ababa, Gondar and South West Ethiopia[(26,27,29)]. In different studies showed this perinatal asphyxia is related to antepartum, intrapartum, and postnatal related factors which increase the risk of neonatal mortality.[36,37]

A mother who did not breastfeed during the first hour of delivery increased neonatal risk of death by the commutative hazard of 4.1 times when compared with those who got breastfeeding during delivery. The association observed between breastfeeding and neonatal mortality in this study is supported by studies done in Gondar, Bahir Dar, and North Shoa.[27,28,38] Breastfeeding was important to boost the immunity of the neonates; therefore, no breastfeeding indicates that the neonates were exposed to infection which increases neonatal morbidity and mortality.

Conclusion

This study revealed that early neonatal mortality is high in the study area. It's recommended that nurses should advocate for the kangaroo mother care method for preterm babies to prevent sepsis. Nurses and physicians should also arrange an appropriate follow-up environment until the end of the neonatal period and increase early detection and management of neonatal infections and problems. It is advisable that those health care professionals need a comprehensive effort to work in the community on the advantage of a balanced diet during pregnancy and the consequence of previous pregnancy bad outcomes to the current pregnancy through antenatal care on the prevention of low birth weight newborns. Health extension workers should also provide health education for the community about early initiation as well as about exclusive breastfeeding during postnatal and antenatal care services.

Acknowledgments

First and foremost we would like to express my deepest gratitude to Wollo University for creating this opportunity. our special thanks also go to Dessie referral hospital human resource management office and neonatal intensive care unit staff members for providing us important information for writing this thesis.

Author contributions

All authors contributed to data analysis, drafting or revising the item, have agreed at the journal to which the object could be submitted, gave final approval for the model to be published, and agreed to be responsible for all components of the work.

Funding

No financial support was provided.

Data Availability

The datasets employed in the current study can be available from the corresponding author upon a reasonable request.

Conflicts of interest

The authors declared no potential competing interest with respect to the publication of this paper.

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Citation: Fissha Y, Milashu M, Haile Y. Time to death and its predictors among early neonatal patients in neonatal intensive care unit of Dessie referral hospital, South Wollo Zone, Northeast Ethiopia. *J Pediatr Neonatal Care*. 2022;12(3):143–149. DOI: 10.15406/jpnc.2022.12.00471