Survival and predictors of early neonatal death in neonatal intensive care unit of Mekelle general and Ayder comprehensive specialized hospitals, Northern Ethiopia, 2018: prospective cohort study

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Abstract

Background: Early neonatal mortality refers to deaths of neonates between 0 and 6 days of life. This contributes three-quarters of neonatal deaths globally. Its predictors vary by country with the availability and quality of health care, which was chosen as the measure of mortality and remains a global public health concern especially in sub-Saharan African countries, including Ethiopia. So the aim of this study is to determine incidence, median survival time and to identify the predictors of early neonatal mortality.

Methods: A prospective cohort study was conducted in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia from January to March, 2018. Data were collected from 253 newborns admitted to the neonatal intensive care unit by interviewing mothers using structured questionnaires and followed for seven completed days of life (day 0 to 6).Kaplan Meier curves were used to estimate survival time, Log-rank test was used to look statistical differences among/between the categories of variables and Cox regression model was used to identify potential predictors of early neonatal deaths. The analysis was conducted using a computer program Stata version 12.

Results: Overall, in this study 32 (12.65%) neonates died which makes the early neonatal mortality rate 126.5 per 1000 live births. The median survival time of early neonates was 2 days. Predictors of early neonatal mortality were very low birth weight (AHR= 3.02; 95 % CI: 1.11, 8.25) and preterm birth (AHR=3.7; 95 % CI: 1.22, 11.188).

Conclusion: This study shows high incidences of early neonatal mortality. Very low birth weight and preterm birth were major predictors for early neonatal mortality. Managing complications of preterm and very low birth weight, preventing preterm delivery and improving quality of services and ensuring a continuum of care are recommended to increase survival of early neonate

Background

The early neonatal period begins at birth and includes the 1st seven days of life(1−3).This is very vulnerable and critical time for neonate survival because high rates of mortality and morbidity in human life present during this period(4−6).Early Neonatal Mortality (ENM) refers to deaths of neonates between 0 and 6 days of life, which uses as the measure of mortality and remains a global public health concern especially in sub-Saharan African countries(7−9).

In 2017globallyunder-five mortality rate was 39 deaths per 1000 live births and 47 percent of these occur during the neonatal period worldwide. Neonatal mortality (NM), accounting for an estimated 2.5 million or 7,000 newborns died every day with the rate of 18 deaths per 1000 live births(10−12)Three-quarters or 75% of neonatal deaths occur in the first week, and more than one-quarter occur in the first 24 hours(13−15).

According to World Health Organization (WHO) report in Uganda neonatal mortality rate (NMR), was under-estimated, which was very high at 29 deaths per 1,000 live births and has not declined over a

period of 15 years. The common causes of neonatal deaths in Uganda are similar to the rest of African countries like Ethiopia, include birth asphyxia, infections and complications of preterm birth16).

The gaps between rich and poor countries were widening: neonatal mortality is now 6.5 times lower in the high-income countries than in low income countries(17).According to Ethiopian demographic health survey (EDHS)2016Ethiopia accounted 29 deaths per 1000 live births of neonatal mortality rate and most of the neonates died in the first week of life(18).

A delay in the identification and treatment of neonatal sepsis leads to the high mortality(20).In developing countries deaths are often not registered and causes of death are not assigned to 99% of deaths(21–23). According to Ethiopian Demographic Health Servey(EDHS)2000 to 2016 neonatal morbidity and mortality continue to be a large component of the burden of disease in Sub-Sahara Africa and its rates reflect a nation's socio-economic status, the efficiency and effectiveness of health care services(24).

Majority of the causes of neonatal morbidity and mortality are preventable. There is a variation in neonatal mortality rate at Neonatal Intensive Care Units (NICU), which importantly reflect variations in quality of care(25).So the purpose of this study was to determine incidence, median survival time and to identify the predictors of early neonatal mortality.

The current global burden of neonatal and child death is largely concentrated in the two regions which account almost 80 % of the newborn deaths. Southern Asia accounted 39 % of all such deaths and sub-Saharan Africa accounted 38 % among newborns. In sub-Saharan Africa, about 1 child in 36 dies in the first month, while in the world's high-income countries the ratio is 1 in 333(11,22).

Regardless of Ethiopia's remarkable success in infant and under–5 mortality, the reduction in neonatal mortality is relatively low. EDHS 2011 reported the Neonatal Mortality Rate (NMR) as 37/1000 live births, which has not shown significant declines from the 2005 EDHS report of 39/1000 live births and in 2016 EDHS report of 29/1000 live births have great reduction but it is still under estimation(11,26).

The causes of neonatal mortality are not well documented in Ethiopia; however, reports from previous studies like a study conducted in Gonder, Northwest Ethiopia identified sepsis, asphyxia, birth injury, tetanus, preterm birth, congenital malformations, and "unknown causes" as major reasons for neonatal mortality but the median survival time of the neonate was not determined (14).

Even though there is a reduction on neonatal mortality that Ethiopia accounted 29 deaths per 1000 live births of neonatal mortality rate and the proportion of NM 43 % and 60.4% in U5M(Under Five Mortality) and in infant respectively, and three quarter (75 %) of these mortality happened in the first week of life, which was also the same in Tigray(24) and the EDHS–2016 showed that there is still a high mortality rate comparing to the target stated in Health Sector Transformation Program (HSTP)10% which is three fold of the target(27).

Different studies have done in Tigray which shows there are still different causes of neonatal mortality in all facility but those studies limited by: these were done before NICU was advanced with technology as well as care, were focused on the neonates both admitted in NICU and in pediatric wards, it was focused on neonate those who delivered by skilled health professionals and were limited to identify early neonatal mortality separately.

Globally half of all neonatal deaths are concentrated in five countries including Ethiopia which accounts 3% (11).Since causes of early neonatal deaths vary by country and with the availability and quality of health care, understanding early neonatal deaths in relation to these factors is crucial.

Understanding of these influences could help to deliver or optimize quality of care for neonates and it will be an input for health workers, hospital management, policy makers and program managers to develop interventions that may reduce neonatal mortality rate. This is also important in order to set health care services more focusing in maternal and child health in addition to strengthen NICU service and may be used to put different interventions.

Methods

Study area and period

This study was conducted in Mekelle general and Ayder comprehensive specialized hospitals, Tigray regional state; which is located at 783km from Addis Ababa (the capital city of Ethiopia) from January to March, 2018. According to Central Statistics Agency 2015,Tigray region has an estimated total population of 5,056,000 with an area of 84,722 km^2(10,54,55).

The Ethiopia health care has a three-tier health-service delivery system. The primary level consists of primary healthcare units (health posts and health centers) and primary hospitals, secondary level services are provided by general hospitals and tertiary services by specialized hospitals. Tertiary level specialized hospital serving for 3.5 - 5 million people, Secondary level general hospital to serve $1 - 1.5$ million catchment populations and Primary level: rural primary hospital60 000 $- 100$ 000 people, health Centre15 000 - 25 000 people and health post3 000 - 5 000 people and urban health center serve for 40 000 people(10).

Study design

A prospective cohort study was conducted among a cohort of early neonates who were admitted to neonatal intensive care unit (NICU) from January to March, 2018 in Mekelle general and Ayder comprehensive specialized hospitals. The minimum follow up time for this study was 7 days until the event of interest occurs (neonatal death).

Source population

All early neonates admitted to neonatal intensive care unit in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia

Study population

All early neonates admitted to neonatal intensive care unit in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia from January to March 2018.

Study subject

Study participants selected by systematic sampling method from early age neonates in neonatal intensive care units of Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia from January to March 2018.

Inclusion and exclusion criteria Inclusion criteria

All early neonates in neonatal intensive care units of Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia from January to March2018.

Exclusion criteria

All neonates' greater ≥7 days of life admitted to neonatal intensive care units

Sample size determination

The general formula for the required number of subjects in a survival study expressed as (56).

$$N = \frac{E}{P(E)} \text{ Where } E = \frac{\left(z_{\frac{\alpha}{2}} + z\beta\right)^2}{P(1-p)\delta^2}$$

WhereE () is the number of events required to be observed in a study, and pE () is the probability of observing an event in a study. δ is log (HR)

Sampling technique and procedure

The study hospitals selected purposely due to the service provision is given with well skilled health providers and better technology that use as referral for the entire region. Two hundred fifty three (253)

study participants also selected proportional from Ayder comprehensive specialized hospital (202) and Mekelle general hospitals (51).

Study variables

The conceptual framework proposed by Mosley and Chen(57),was used in this study to identify and classify the factors that potentially influence ENM.

Dependent variable

Early neonatal mortality was categorized into 'Yes' if the neonate died 'No' if the neonate censored. Censored births were the neonates, who were alive at the end of follow up.

Independent variables

The independent variables in this study were demographic and socio-economic, maternal, delivery factors, neonatal factors, and NICU factors.

Data Collection Procedure

Data collection in NICU was carried out prospectively by interviewing mothers using structured questionnaires and from the medical record charts using the data extraction checklist of the neonates by trained nurses. During the process, the principal investigator was supervised these trained data collectors and assisted by intensive care unit head nurse. The questionnaire was derived from WHO standard verbal autopsy questionnaires(8). The questionnaire was initially developed in English and translated into local language, Tigrigna. One nurse that can speak the local language from each hospital was assign for data collection. The data collectors were collected information by interviewing all mothers whose neonate admitted to NICU of Mekelle general and Ayder comprehensive specialized hospitals from 0–6days of life and the clinical information was extracted from medical record charts and by assessment of neonates. The mother and neonate follow for seven days and whenever the neonate discharged to home data collection was completed using phone call. Data collection included demographic and socio-economic characteristics, maternal, delivery, new born and NICU factors. The outcome variable was death in the first 0–6 days after birth.

Data Quality control and management

Various efforts were made to assure the data quality. Personal supervision especially in the data collection process, training was given to data collectors about the research protocols and also oriented on how to appropriately collect the data. Data quality process starts from the check list to the computer

entry. The principal investigator inspects all the performances of the data collectors and measure data. Before the data were entering, it was checked for completeness and consistency by the PI.The process of data generation and entry was under close supervision of the investigator. Data were cleaned, sorting and analysis using STAT software version 12.

Data analysis

Death of neonate was the event of interest and the coding were "1" for death and "0" for censored. The survival time was calculated in days using the time interval between the date of birth and the date of death. Information about the number of deaths before seven complete days after birth and right-censoring (survival beyond seven days).Data was entered; cleaned, recoded and analyzed using STATA Version 12 statistical software. The statistical analysis of survival was based on Cox proportional hazards regression model. Cox-proportional hazard model was used to identify the predictors of early neonatal death. The Cox proportional hazards model is such a model: $H(t) = h0(t) \exp(\beta_1 x_1 + \cdots + \beta_k x_k)$ (58,59).

Descriptive statistics used to describe the frequencies, percentages, rates and to calculate the mean and standard deviation after checking the distribution of the data. Kaplan Meier curves were used to show the pattern of death, estimate probability of survival and to compare the survival curves. Log-rank test was used to look statistical differences among or between the categories of variables to be included in the Cox-proportional hazard model. Cox regression model was used to identify potential predictors of early neonatal deaths.

In the Univarete or Bivariate Cox analysis the covariates; residence, mother educational status, number of newborn, distance from health facility, Birth weight, Gestational age, Apgar score in one minute, sex, admission diagnosis and medication were identified as statistically significant at p_ value ≤ 0.25 level of significance. These significant explanatory variables were included in the Cox-proportional hazard model to identify potential predictors of ENM.

After confounding variables were identified, the variables with p-values of 0.05 or less were retained in the final model analysis.Confounding and effect modification was checked by looking at regression coefficient change if greater than or equal to 15 % and multi-co linearity was checked using variance inflation factor and value of <10 was used as a cutoff point, indicating no co linearity.

Proportional hazard assumption was tested by using covariate specific proportional hazard assumption test. Residuals were checked using graphs and goodness-of-fit test by Cox Snell residuals. Upon the finding HR and 95% CI interpretation for statistically significant predictors were perform.

Operational definitions

Birth asphyxia/shortness of breathing: Any respiratory problem, fast breathing, and or difficulty of breathing.

Early Neonatal Mortality: Defined as the probability of dying between (0–6) days or before seven completed days of life.

Premature: Any viable neonate before term (<37weeks of gestation)

Results

Response rate and Socio-demographic characteristic

Response was obtained from all participants (n = 253), out of these 233(92.09) were married,53 (20.95%) of the live births were from teenager mothers (below the age of 18 years) and those neonates born from these mothers 21(39.62%) of them exposed to preterm.88 (34.78 %) of the mothers had completed secondary school and 19 (7.51 %) of the mothers had run their own business and employee in governmental organizations (Table1).The current age of the mother was normally distributed with mean and standard deviation of 24.96 (SD = ±4.3).

Maternal and pregnancy characteristics

Among the total mothers recruited into the study, 30 (11.86 %) of the mothers had previous history of abortion and 6 (2.37 %) of the mothers had a history of still birth. From the total 25 multiple births 19 (76.00%) of them were exposed to preterm births. Regarding medically diagnosed diseases, 28 (11.1 %) had medically known disease. Of these, diabetes mellitus had highest prevalence 8 (28.57 %) (Table2).

Neonatal and Neonatal Intensive Care Unit characteristics

Regarding the neonatal characteristics, the male to female ratio was 1.3:1. One hundred two (40.32%) were preterm and 151 (59.68%) term babies. Around half, 139 (54.2 %) of neonates received antibiotic Treatment and 74 (29.2 %) were EONS case neonates. Among all 31(12.3 %) of the neonates have birth defect (Table 3).

Survival analysis and outcome of the follow up

Neonates were followed up for 1425.32 total analysis time at risk, at risk from t = 0 neonate-days. The median survival time of early neonates admitted to NICU was 2 days. In the study, 5 (15.62%) of neonatal deaths occurred in the first 24 hours, 7 (21.88 %) in the next date of birth and18 (56.25%) death occurred within the first 72 hours. The cumulative survival rate of neonates at the end of the follow up were 86.96 %(95% CI: 0.8197, 0.9065) (Table 4 and Fig.1). Overall, in this study 32 (12.65%) neonates died which makes the ENMR 126.5 per 1000 live births. At the end of follow up, 221(87.4 %) were alive. The leading

cause of death were 13 (40.6 %) Respiratory distress, 11(34.3 %) premature complication, 3 (9.3) low birth weight, 3 (9.3%) asphyxia and 2 (6.25 %) aspiration pneumonia. One hundred eighty (71.1%) were completed their follow up time in the hospital where as 73 were completed their follow up outside.

Bivariate and Multivariable analysis

Log-rank test showed that there is a significant difference of survival experience among groups of residenceX^2 for Log rank test = 2.25,p = 0.1335,mother educational statusX^2 for Log rank test = 4.47,p = 0.2149, number of newbornX^2 for Log rank test = 6.12,p = 0.0134, distance from health facilityX^2 for Log rank test = 3.42,p = 0.0643, Birth weightX^2 for Log rank test = 3.42 ,p = 0.0643, Gestational ageX^2 for Log rank test = 22.25,p = 0.0000, Apgar score in one minuteX^2 for Log rank test = 11.20 ,p = 0.0037, sex, admission diagnosis and type of medication(Table 5).

Multivariable analysis revealed that a neonate born with very low birth weight (1000−1499gm) had 3 times higher hazard of neonatal death compare to neonates born with normal birth weight (2500−3500 gm) (AHR: 3.02, 95 % CI: 1.11,8.25).Neonates who were born with gestational age less than 37 weeks had 3.7 times higher hazard of neonatal death than neonates who were born with gestational age greater than 37weeks,(AHR = 3.7;95 %CI:1.22,11.19).

Effect modification and Multicollinarity were assessed in this study, no confounding effect was observed. No covariates violated the proportional-hazard assumption test. For the residual test, it concludes that the final model fits the data very well. These residuals should have a standard censored exponential distribution with hazard ratio. The hazard function follows the 45° line very closely (Fig. 2).

The final Cox regression analysis model for the outcome of early neonatal death demonstrated. Its association with very low birth weight (1000−1499gm) (AHR = 3.02, 95 % CI: 1.11, 8.25) and Neonates who were born with gestational age less than 37 weeks (preterm) (AHR = 3.7; 95 %CI: 1.22, 11.19) (table 6).

Discussion

The aim of the study conducted is to assess survival and predictors of early neonatal death in neonatal intensive care unit in order to set health care services more focusing in maternal and child health in addition to strengthen NICU service and may be used to put different interventions.

In this study, ENMR was found to be higher (126.5 per 1000 live births) than the national average that is 29 per 1000 live births EDHS2016. The higher rate could be explained by the fact that this study was done in NICU those newborn babies in need of critical medical attention was admitted while the national average includes both high-risk new born babies and normally new born babies. This rate is similar with other studies conducted in Cameroon due to both studies conducted in NICU and with the same age group(32), but unlike this study ENMR is different in different studies like Sudan included neonates born

in the study hospital and admitted to nursery unit with incidence rate of 6.6% and China 7.9% incidence rate conducted retrospectively in the rural community while this study included home delivery admitted to NICU and included the rural and urban residence (2,23,51).

This study showed that there is higher rate of mortality than data extracted from HDSS in Kersa /eastern Ethiopia which was 19.55 per 1000 and other countries like Brazil (33,51,60).The discrepancy could be explained in terms of the place where information was gathered. Different studies conducted before in Sudan, Iran, China, Brazil, Cameroon, Indonesia and Ethiopia had revealed that most neonatal deaths occurred in the first 24hr and in the first week of life which is similar to this study (2,4,14,22,23,29,30,32,51,52).These findings could be associated with prematurity and low birth weight in which the NICU set up was impair to manage these risk factors during this period.

Studies conducted in Gonder and Nigeria reported that most neonates died in their first week of life because of complication occurring during pregnancy but this study indicates most early neonatal death occurred because of preterm and very low birth weight this deference might be because of demographic characteristics of the respondents, poor quality of antenatal care, delay in identification and poor management of complications during pregnancy(14,31).

In this study relatively the major reason to early neonatal mortality is found 13 (40.6 %) Respiratory distress, 11(34.3 %) premature complication, 3 (9.3%) low birth weight, 3 (9.3%) asphyxia and 2 (6.25 %) Aspiration pneumonia, this is similar with finding of study from northern Ethiopia that was, asphyxia, infection, and prematurity were the leading causes of death at 35, 23, and 23% respectively (61).

In this finding log rank test analysis result shows the covariates like residence, mother educational status, number of newborn, distance from health facility, Birth weight, Gestational age, Apgar score in one minute, sex, admission diagnosis and medication were statistically significant to survival or time to death. This is in line with study in Cameron which was Preterm birth, Asphyxia and acute respiratory remained significantly associated with neonatal mortality (32).

This study multivariable analysis identified that prematurity and very low birth weights were associated with increased hazard of neonatal death. These were contributing to ENM with AHR: 3.7 and 3.02for premature and very low birth weight respectively. Preterm birth accounted for most early neonatal deaths and also preterm birth complications were the leading cause of death in all regions of the world (62).The characteristics of mothers whose VLBW babies had died showed the strong influence of the social component and access to care on perinatal outcomes, which is consistent with a recent systematic review (63).

This study has revealed that prematurity was the predominant cause for early neonatal mortality which is similar with different studies conducted before in Sudan, Saudi Arabia, Pakistan, Northeast Brazil,Southern Brazil, Indonesia and Eastern Ethiopia(2,3,5,13,29,30,33,51,52).

The current study finding showed that neonates with a very low birth weight experienced higher mortality. This finding is similar to studies conducted in Ethiopia and different parts of developing countries like Iran, Nigeria and Indonesia(4,15,52,61). The male predominance in this study is consistent with other studies done in Gonder; Sub Saharan Africa and Northern Ethiopia. This indicates that male neonates are more vulnerable during the neonatal period, a finding in agreement with the well described biological survival of girls in the neonatal period. It could also be as a result of preference for male child by some culture (14,15,20,28).

These findings showed that neonates born preterm with very low birth weight had a higher chance of death. This is similar to previous studies reported on preterm with very low birth weight related to high risks of ENM in Brazil(3,29).

This study showed that having low birth weight have a protective effect on ENM. Hence, this study indicated that managing low birth weight is possible, which may be related to timely admission to NICU and the focus of pediatricians on neonates with low birth weight and the NICU set up also appropriate to manage low birth weight neonates.

A systematic review from 60 low and middle income countries using population based nationally representative surveys revealed twins had around 3 times increased odds of death compared to singletons after adjusting for birth weight. A caesarian section was associated with a significant protective effect in twins. Institutional deliveries and increased access of caesarian sections may be considered for twin pregnancies in low- and middle income countries to decrease early adverse neonatal outcomes (19).

In accordance with this findings, in general, a study conducted in northern Brazil show that preterm and very low birth weight was associated with ENM (29). In this study the cumulative survival rate of early neonates at the end of the follow up were 86.96 %(95% CI: 0.82, 0.91). Overall, the study shows 32 (12.65 %) neonates died at first week of their life and this is higher than from Brazil which is 4.7% died in the same time period; this difference might be due to proximal causes, Low social standard, Lack of education, unplanned or unintended pregnancies and late attendance for Antenatal Care (64).

The strength of this study is that, it was assessed all predictors of ENM, data collection was also complete and reliable because it is a prospective cohort and the study area covers hospitals with high patient flow that those hospitals give service for all referred from all health institutions of Tigray, so we can conclude that it is representative for the entire region. One major limitation of the study was unavailable waiting room for mothers that lead unable to get them easy.

Conclusions

This study shows high incidences of ENMR and the median survival time was two days. Preterm birth and very low birth weight were the major predictors of early neonatal mortality. Multiple births were highly exposed to preterm births.

Recommendations

Governmental and Non-Governmental Organizations

- TRHB and other stakeholders should give special emphasis to manage preterm birth and very low birth weight because both predictors and final causes of death related with preterm complications.
- Ensure essential equipment and commodities are consistently available

Institution level

- Improved obstetric care, antenatal quality of service and identification of women who are likely to deliver less than 37 weeks of pregnancy and treatment with corticosteroids several days before delivery to prolong their pregnancy and speed up maturation of fetal lungs and further reduce incidence of prematurity
- The institution should ensure the attendant of pediatricians in every delivery for timely resuscitation of babies at birth. This will go a long way to reduce high case fatality and morbidity related to neonatal mortality in the first few hours of life.

Community level

- Create awareness for those multiple pregnant mothers to come to health facility before the onset of labor to reduce preterm delivery.
- Kangaroo mother care for very low birth weight babies should be well informed and practiced in the community

Future studies also need to assess the level of awareness, treatment and control of these risk factors.

Abbreviations

ACSH: Ayder Comprehensive Specialized Hospital; ANC: Antenatal Care; CS: Cesarean Section; EDHS: Ethiopian Demographic Health Survey; ENM: Early Neonatal Mortality; ENMR: Early Neonatal Mortality Rate; EONS: Early Onset Neonatal Sepsis; GA: Gestational Age; HR: Hazard Ratio; HSTP: Health Sector Transformation Plan; MGH: Mekelle General Hospital; MNCH: Maternal, Neonatal, and Child health; NICU: Neonatal Intensive Care Unit; NM: Neonatal Mortality; PI: Principal Investigator; RDS: Respiratory Distress Syndrome; R&w: Read and Write SCBU: Special Care Baby Unit;R&W:Read and Write SDGs: Sustainable Development Goals; TRHB: Tigray Regional Health Bureau; TT: Tetanus Toxoid (TT); U5M: Under Five Mortality; UNICEF: United Nations International and Children's Emergency Fund and VLBW: Very Low Birth Weight

Declaration

Ethics approval and consent to participate

Ethical approval of the research was issued from the Research Ethics Review Committee of College of health Science, Mekelle University collage of health science to Ayder comprehensive specialized hospital and Mekelle general hospital, after getting permission from hospital administrations, the request letter was written for the concerned bodies of respective departments. Following this, searching and obtaining of the selected samples' medical record were processed with assigned person. Finally, strict care for the patients' medical records and the confidentiality of records that can identify study participants was protected. These have been achieved through anonymousity and by abandoning the individually identifiable information, which specifically refers to identity of patient like MRN and coding was used instead.

Ethical clearance was obtained from Mekelle University, College of Health Sciences Ethical review board. Permission letters were also sought from Tigray Regional Health Bureau. Written Informed consent from the mother was obtained after clear explanation of the purpose of the study. Confidentiality and anonymity was maintained.

Consent to publish

I agree to rules and regulation of the BMC Pediatrics.

Availability of data and materials

The datasets used and/or analyzed during the current study are availablefrom the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AH conceived the research, wrote the draft manuscript, carried out the analysis and interpretation. LG drafted the manuscript and revised it critically in the design and analysis of the research. HT was involved mainly in statistical analysis, design and revising in draft of the manuscript. TH was involved in revising the design and analysis of the research.

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Tables

Table 1 Demographic and socio-economic characteristics of mothers whose early neonate admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018(n=253)

Characteristics		Freq.	Per.
Residence	Urban	157	62.06
	Rural	96	37.94
MA at first birth	<20years	58	22.91
	20-24years	124	63.58
	>24years	71	36.41
MA on marriage	< 18years	53	20.95
	≥18 years	200	79. 05
Religion	Orthodox	243	96.05
	Muslim	6	2.37
	Other	4	1.58
Maternal marital status	Married	233	92.09
	Single	20	7.90
Mother Educational status	primary school	78	1.58
	unable to R&w	49	19.37
	Secondary	88	34.78
	Tertiary	38	15.02
Occupational status	House wife	183	72.33
	Student	10	3.95
	Own business	19	7.51
	Governmental	41	16.21

Table 2 Maternal related characteristics of early neonates admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018 (n=253)

Characteristics		Freq.	%
Number of new born	Singleton birth	228	90.12
	Multiple birth	25	9.88
Gravidity	One pregnancy	111	43.87
	Two pregnancy	67	26.48
	≥Three pregnancy	75	29.64
History of Abortion	Yes	30	11.86
	No	223	88.14
No. of abortion	Zero	223	88.14
	One	22	8.70
	Two	8	3.16
Mother health problem	Yes	28	11.07
	No	225	88.93

Table 2 Characteristics of mothers whose early neonate admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018 (n=253) **(Continued)**

Characteristics		Freq.	%
Delivery complication	Yes	72	28.46
	No	181	71.54
If Yes, No. of TT injection	≥ 2 injection	170	67.19
	1 injection	70	27.67
RH Factor	Positive	243	96.05
	Negative	10	3.95
RVI Status	None reactive	239	94.47
	Reactive	14	5.53
Use of ANC service	Yes	225	88.93
	No	28	11.07
Number of ANC Visit	<4 visits	67	26.48
	≥4 visits	186	73.52
Distance to HF	≤10 km	171	67.59
	>4 km	82	32.41
Mode of delivery	SVD	178	70.36
	Cesarean section	75	29.64
Place of birth	Hospital	203	80.24
	Health Center or Clinic	39	15.42
	Home	11	4.35

Table 3 Neonatal related characteristics of early neonates in NICU of Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018 (n=253)

Characteristics		Freq.	%
Birth weight	NBW(2500-3500gm)	141	55.73
	LBW(1500- 2499gm)	67	26.48
	VLBW (1000- 1499gm)	45	17.79
Gestational age	Term(≥37 weeks)	151	59.68
	Preterm (<37 weeks)	102	40.32
Apgar score in one minute	7-10	129	50.99
	<7	49	19.37
	un known	75	29.64
Sex	Male	143	56.52
	Female	110)	43.48
Initiation. of BF within one hr	Yes	20	7.91
	No	79	31.23

Table 3 Neonatal related characteristics of early neonates in NICU of Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018 (n=253) (Continue)

Characteristics			Freq.	%
Admission diagnosis		EONS	79	31.23
		Hypothermia	36	14.23
		Preterm	51	20.16
		MMC	22)	8.70
		Others	65	25.69
Birth defect		Yes	35	13.83
		No	218	86.17
Hospital type		ACSH	202	79.84
		MGH	51	20.15
Kind of Medication		Antibiotic	139	54.94
		ABCs'	37	14.62
		KMC	22	8.70
		Radiate Warmer	34	13.44
		Others	21	8.3
Outcome status		Alive	221	87.35
		Death	32	12.65
Primary Cause of neonatal death		Respiratory distress	13	40.6
		Birth Asphyxia	3	9.3
		Preterm Complication	11	34.3
		Aspiration Pneumonia	2	2.65
		L BW Complication	3	9.3

Table 4 Survival analysis of early neonates during follow up time those who admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018 (n=253)

Time Interval	Total	Death	Lost	Survival Probability%	(95% Conf.int.)
0-1	253	5	0	98.02	95.32,99.17
1-2	248	7	0	95.26	91.80,97.28
2-3	241	6	0	92.89	88.94,95.46
4-5	235	1	0	92.49	88.48,95.14
5-6	234	12	0	87.75	83.03,91.22
6 -7days	222	1	221	86.96	81.97,90.65

Table 5 Log rank test result of early neonates admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018   (n=253)

Variable	Log rank(X^2)	P-value
Residence	2.25	0.1335
Marital status	0.14	0.7035
Mothers age on marriage	0.56	0.4554
Religion	1.68	0.4306
Mother educational status	4.47	0.2149
Occupational status	3.30	0.3480
Age of mother at first birth	0.38	0.825
Number of new born	6.12	0.0134
Birth interval	0.01	0.9971
Use of family planning	0.07	0.7902
Method of family planning use	1.36	0.7159
Gravidity	1.11	0.5729
Still birth	0.06	0.8131
Sibling mortality	0.31	0.5787
Mother diagnosis	0.73	0.3914
Type of diagnosis	2.95	0.5669
Delivery complication	0.56	0.4531
Type of complication	0.78	0.9784
Tetanus antitoxin	0.98	0.3232
Number of TT injection	2.52	0.2829

Table 5 Log rank test result of early neonates admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, 2018 (n=253)(Continue)

Variable	Log rank(X^2)	P-value
RH Factor	0.58	0.4465
Initiation of BF within a hour	0.11	0.7409
RVI Status	1.15	0.2837
Use of ANC service	0.99	0.3199
Number of ANC Visit	0.45	0.50234
Distance to Health Facility	3.42	0.0643
Mode of delivery	0.33	0.5678
Place of birth	2.89	0.2356
Delivery assistance	0.43	0.8060
Birth weight	54.84	0.0000
Gestational age	22.25	0.0000
Apgar score in one minute	11.20	0.0037
Sex	2.30	0.1297
Admission diagnosis	9.58	0.0480
Birth defect	0.49	0.4849
Kind of Medication	8.05	0.0897

Table 6 Multivariable Cox-proportional hazard model on predictors of ENM in Mekelle general and Ayder comprehensive specialized hospitals

| Characteristic		Un Adjusted HR	95% CI	Adjusted HR	95% CI
Residence	Urban	Ref.			
	Rural	1.68	0.84,3.36		
Mother Educational status	Primary school	Ref.			
	Un able to R&W	.82	0.30,2.23		
	Secondary school	.53	0.20,1.38		
	Tertiary	1.51	0.60,3.75		
No. of New born	Singleton birth	Ref.			
	Multiple birth	2.73	1.18,6.32		
Distance	≤10 Km	Ref.			
	>10Km	1.89	0.94,3.79		
	Normal BW(Ref.)	Ref.			
Birth Weight	Low B W	0.41	0.09,1.88	0.23	0.05,1.12
	Very Low BW	7.30	3.41,15.63	3.02	1.11,8.24
GA	Term(Ref.)	Ref.			
	Preterm	5.83	2.52,13.49	3.69	1.22,11.18
Apgar score in one minute	Apgar 7-10	Ref.			
	Apgar less	3.13	1.43,6.86		
	Unknown	1.02	0.40,2.59		
Sex	Male	Ref.			
	Female	0.56	0.26,1.19		

Figures
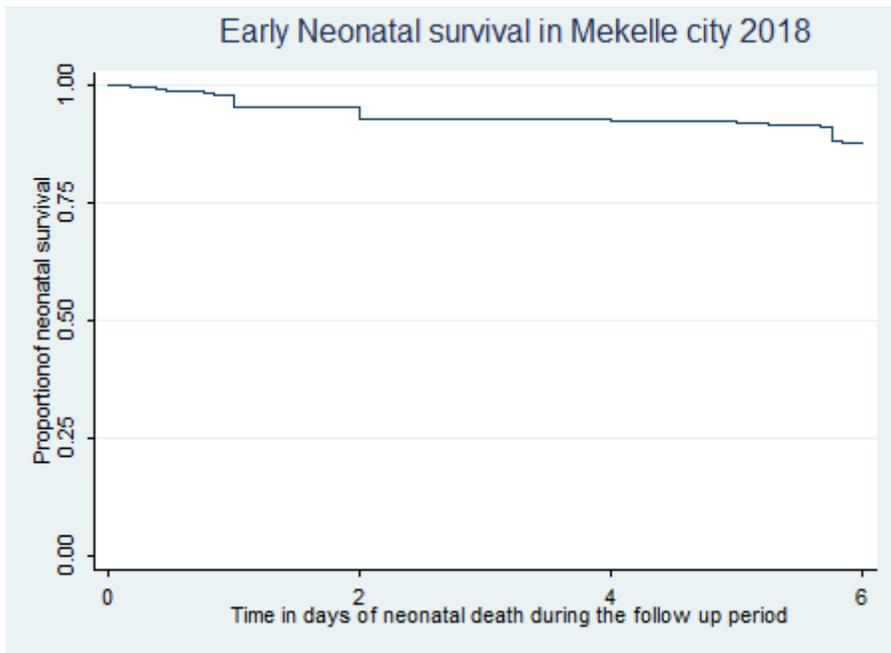
Figure 1

Kaplan Meir survival estimate on the survival time of early neonates admitted to NICU in Mekelle general and Ayder comprehensive specialized hospitals, Tigray, Ethiopia, January - March, 2018 (n=253)
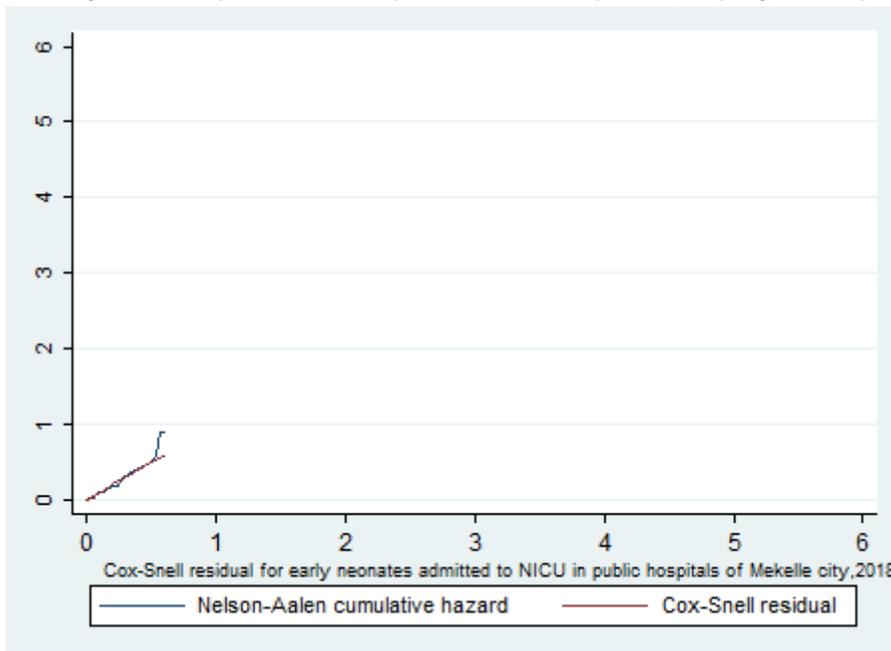

Figure 2

Cox Snell residual Nelson-Alen cumulative hazard graph on early neonates' in NICU of Mekelle general and Ayder comprehensive specialized hospitals, Tigray region, Northern Ethiopia, 2018.