Incidence and Determinants of Newborn Mortality in the First Three Days of Delivery in Northwestern Ethiopia: A Prospective Cohort Study

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Abstract

Background: Addressing the target of sustainable development goals of reducing perinatal mortality was still a global challenge, and it is a concern in Ethiopia. Therefore, this study planned to determine the incidence and determinants of neonatal mortality in the first three days among babies delivered in Amhara Regional State's referral hospitals.

Methods: A hospital-based prospective cohort study design was conducted among 810 neonates in the first three days of delivery between March 1 and August 30, 2018. The neonates were followed, starting from the time of admission to 72 hours. An interviewer-administered questionnaire and medical record review were conducted for data collection. Data were entered into Epi-data manager version 4.4 and analyzed using STATA™ version 16.0 for the analysis. Cox-Proportional hazard model was used to determine the survival time of the newborns.

Results: The overall incidence of newborn mortality in this study was 151/1,000 births. Neonatal mortality was significantly high among newborns whose mothers came between 17 and 28 weeks of gestation for the first visit; among those whose mothers labour was not monitored with a partograph, mothers experience postpartum haemorrhage, develop fistula in the first 24 hours, and experience obstructed labour. However, 39% were less risky among newborns whose mothers were directly admitted and whose mothers had visited health facilities in less than 1-hour, both.

Conclusions: This study revealed that about 1 in 7 newborns died in the early three days of life. Timing of the first antenatal visit, quality of labour monitoring, maternal complications, and delay in seeking the care were the determinants. Thus, scaling-up of evidence-based interventions and harmonized efforts to improve antenatal care quality, promote institutional deliveries, provide optimal essential and emergency obstetric care, and ensure immediate postnatal care may improve neonatal survival.

Background

The newborn period is critical in the miracle of life and death. In 2018, the global neonatal mortality rate was estimated at 18 deaths per 1,000 live births, and there were 28 deaths per 1,000 live births in Sub-Saharan Africa [1] and 30 deaths per 1000 live births in Ethiopia [2]. According to a systematic review in developing countries, despite more than 99% of neonatal deaths in low and middle-income countries, these settings lack the exact timing of either overall or cause-specific neonatal deaths [3]. The same systematic review also revealed that 57% of neonates die in the first three days of life, and two-thirds of these deaths occur within the first 24 hours. Furthermore, this review indicated that among 52% of under-five mortality in the Southeast Asia region, one-third of the neonatal mortality occurred within the first three days of life. Among 30% of the under-five deaths in the World Health Organization (WHO) African region, 17% of the deaths occur within the first day of life [3]. The WHO also confirms that the death risk is the peak in the first 24 hours of life, and more than half of deaths and about three-quarters of all neonatal deaths occurred within the first week of life [4]. In Ethiopia, a study conducted at a referral

specialized teaching hospital revealed that the death of babies who came between the age of 1–3 days was riskier than 4–7 days [5].

It has been suggested that the scaling-up of evidence-based interventions that begin at the antenatal period, coordinated efforts aimed at improving the quality of antenatal care, promoting institutional deliveries, providing optimal essential and emergency obstetric care, and ensuring immediate postnatal care of neonates are essential in low and middle-income countries [3, 6]. Consequently, some countries, including Ethiopia, have substantially improved targeted coverage for some interventions. However, these coverages have not resulted in the expected magnitude of reduction in neonatal mortality rate, specifically neonatal mortality within the first three days of life. The possible reasons were the provision of suboptimal quality of care in health facilities and the lack of concomitant increase in the coverage of the critical interventions in the continuum of care [3]. For example, a recent study in Ethiopia indicated that only 12.1% of women completed the continuum of maternal care services, and 25.1% did not receive any care during their recent births [7].

Though the definition of perinatal mortality rate (PMR) starts from 28 weeks of gestation in low and middle-income countries (LMICs), the mortality rate is higher than the developed countries that stated the definition from 20 weeks gestation. The perinatal mortality rate includes all stillbirths and neonatal deaths in a given period over the total number of births multiplied by thousand [8]. In LMICs, there is a lower preterm newborns' survival rate, and the numerator for PMR includes all fetal deaths with the gestational age of 28 weeks and above and all neonatal deaths within seven days of life [8]. However, according to a global network study, In LMICs registries, most neonatal deaths occurred in babies > 37 weeks gestation, weighed at least 2500 grams, shortly after birth [9]. Previous studies also identified multiple risk factors of PMR in LMICs [10–14]. Among them, poverty is an underlying cause of many neonatal deaths either by increasing the prevalence of risk factors such as maternal infection or reducing access to adequate care [15]. Studies also revealed that the proportions of PMR's common causes such as prematurity (17%); asphyxia (25%); infection (37%); tetanus (7%); diarrhoea (3%); congenital malformations (4%); and other causes (7%) [16–19]. Almost all the studies were conducted either at the community level and within 28 days of life and recommended prevention through better medical care and hospitalization in the intrapartum and early neonatal period [9].

However, to the best of the author's knowledge, despite a significant number of deaths within the first three days, there is a paucity of data in the first three days of life, particularly at the tertiary level of care. Neonatal mortality rates and determinants in the early neonatal period (the first three days of life in this case) are essential for arranging programs and identifying suitable interventions. Local and recent evidence about the problem's spread could help implement programmatically relevant decision-making [10]. Moreover, since both biology and empirical data suggest that the cause of death distribution differs substantially between these periods, separate cause-of-death estimates are required for the first three days of life, within the first seven days, and within 28 days of life [10]. Therefore, this study aimed to address the incidence and determinants of newborn death in the first three days of life among babies delivered in referral hospitals.

Methods

Study setting and period

This study was conducted at the maternity wards of referral hospitals in Amhara Regional State between March 1 and August 30, 2018. The National Regional State is located between 9° 20' and 14° 20' North latitude and 36° 20' and 40° 20' East longitude in the Northwestern part of Ethiopia. According to the Central Statistics Agency, the projected total population estimate Amhara Region in 2020/21 is 22,536,999 (11, 236, 853 males, 11, 300,146 females). Of which 20.08% were urban residents [20]. As per the annual performance report published by the Federal Ministry of Health (MOH) of Ethiopia in the 2009 Fiscal Year, the region had 68 hospitals, 841 health centres, and 3342 health posts [21]. At the time of data collection for this study, among the 68 available hospitals in the region, Dessie, Felege-Hiwot, University of Gondar, Debre-Birhan, and Debre-Markos were referral hospitals. Each referral hospital is assumed to render services for 5 million people. The selected three referral hospitals were the University of Gondar Teaching Referral Hospital, Felege Hiwot Referral Hospital, and Debre Markos Referral Hospital.

Several health professionals have been produced from the university of Gondar for more than half a century ago. Gondar city is also located 727 km away from Addis Ababa and 180 km from Bahir Dar. This hospital provides services to the population in the surrounding area of Gondar town and the nearby zones. Paediatrics and child health departments provide services for rural and urban populations and include outpatient clinics, an emergency department, pediatric and malnutrition wards, and neonatal intensive care units (NICU). The NICU was established 20 years ago and served as a tertiary and a referral unit for the region. High-risk babies delivered within the institution, referrals from other health facilities, and referrals from home deliveries receive care from the university of Gondar hospital (UoGH) NICU. Though there is a seasonal variation in the number of neonatal admissions, the annual average admission rate is 1,140. This 32-bed capacity NICU has radiant warmers and nine incubators. The NICU does not have a mechanical ventilator or continuous positive airway pressure (CPAP) machine. However, bubble CPAP that is locally developed for neonates with respiratory distress syndrome (RDS). Also, for term neonates, there are four incubators and three phototherapy machines. The babies receive oxygen through the attached nasal prongs or a nasal catheter with oxygen cylinders or oxygen concentrators. The commonly used antibiotics for the empirical treatment of sepsis are ampicillin and gentamicin. Medications are administered via a peripheral vein, and in few cases, the umbilical vein is used. A total of four rooms are found in the NICU, which is useful for preterm babies, for term babies, for communicable diseases, and for the maternity side at which relatively stable neonates and babies who need kangaroo mother care. The NICU runs with seven medical interns, two pediatric residents, one paediatrician, and 17 nurses[22].

Similarly, the Felege-Hiwot is located 578 km away from Ethiopia's capital, Addis Ababa North West. This referral hospital serves the population around the Bahir Dar special zone, west Gojjam zone, Awi zone, South Gondar Zone, and a teaching hospital for the Bahir Dar University. These zones are the residences

of more than 7 million people. Felege Hiwot referral hospital officially commenced its function in 1963, and currently, it delivers health care services with medical, surgical, gynaecological, orthopaedic, intensive care units, paediatrics, and ophthalmological wards with a total of 375 beds and 561 staffs. Annually, nearly 6300 neonates were seen with different health problems. The neonatal unit has 60 beds, five paediatricians, and 20 nurses [23].

Furthermore, Debremarkos referral hospital is located 300 km from Addis Ababa, Ethiopia's capital, and 256 km from Bahirdar. This hospital is the only referral hospital found in East Gojjam Zone and serves as a teaching hospital for Debre Markos University. This hospital is providing services for more than 3.5 million people in its catchment area. The hospital also provides neonatal intensive care services for critically ill neonates and those who need neonatal care. The NICU has 27 nurses, one paediatrician, and two general practitioners. The unit has 10 NICU beds, four kangaroo mother care beds, 19 mother side beds, eight radiant warmers, and six incubators. The NICU's standard nursing procedures are phototherapy, umbilical transfusion, oxygen administration, nasogastric tube insertion, intravenous infusion, urinary catheterization, lumbar puncture, and CPAP. In 2017, this hospital provided neonatal intensive care services for 1419 neonates [24].

Study design and population

An institution-based prospective cohort study was conducted among a cohort of term pregnant mothers, and newborns admitted to three systematically selected referral hospitals. All term pregnant mothers ($\geq$ 37 weeks gestational age (GA)) were admitted to the selected referral hospitals included in this study. Then, followed up until they gave birth, and their neonates were followed up for a total of 72 hours. Additionally, neonates discharged with an appointment and normal status were followed using mothers' phones and the nearby health extension workers until three days of life. Cohorts of newborns who were delivered from women aged 15–49 years were included. On the other hand, those delivered from women with mental illness and unable to hear and talk due to illness and twins were excluded from the study.

Sample size and sampling technique

The sample size of 832 was calculated using Epi-info version 7 stat calc software. The following assumptions of the incidence ratio of early neonatal death of 369 per 2142 deliveries [25], 95% confidence level, the margin of error 2.75, and 15% lost to follow-up.

Systematic random sampling was used to identify 832 admitted term pregnant women enrolled in the follow-up study. First, a simple random sampling (i.e., lottery method) technique was employed to select the three hospitals. The study subjects were then allocated with the proportion of the expected admitted number of term pregnant women per referral hospital, 300 each for UoGH and FHH, and 210 for DMH. Then, the calculated sample was selected consecutively from each referral hospital.

Variables

Times-to-event, the event of interest was early neonatal death and dichotomized as (alive = 1 and died = 0). The determinant variables included socio-demographic and economic factors: ethnicity, religion, place

of residence, marital status, education status of the mother, and occupational status of the mother, age of mother, maternal and neonatal related factors: ANC follow up, parity gravidity, mode of delivery gestational age, birth weight, age of neonate at discharge, and sex of neonate. Neonatal illnesses include respiratory distress, perinatal asphyxia, sepsis, congenital malformation, hyaline membrane disease, and meconium aspiration syndrome—care/ service-related factors: Partograph follow-up, length of stay, and obstetric complications.

Data quality assurance and questionnaire

First, we prepared the English questionnaire, translated to Amharic's local language, and back to English by different individuals to check its consistency. The survey was pretested on 42 mothers (14 exposed and 28 unexposed cohorts) in Debre Tabor Hospital, which differs from the study hospitals. The questionnaire (Appendix 1) was then assessed for its clarity and completeness. Some skip patterns were corrected, and questions difficult to ask were rephrased. The questionnaire had three parts. The first part was socio-demographic factors (i.e., maternal age, body mass index, age at first marriage, age at early pregnancy, age at first delivery, ethnicity, residence, marital status, educational status, husband educational status, occupation, an estimated distance of home from health institution, determining range from primary health institute to referral hospital, religion, and income). The reproductive factors constitute the second part, like gravidity, parity, gestational age, referral status, birth attendant, previous cesarean section, mode of final delivery, antenatal care attendance, number of ANC visits, duration of labour before the presentation, prior history of abortion, and obstetric complications. The third part was that programmatic factors included infrastructure and transportations. The completed questionnaires were checked day-to-day for inclusiveness, correctness, clarity, and consistency by the supervisors and the principal investigators, and necessary corrections and changes were made. During data entry and analysis, complete and consistent variables were checked using frequency distributions, cross-tabulations, sorting in ascending, and descending order.

Data collection process

Because of day and night allocation of data collectors in each hospital, six bachelors (two per hospital) holders experienced midwives collected data interchangeably (by shift), and three general practitioners (1 per each hospital) were supervised the process. Based on the focus on the study's objective and the value of collecting the actual data, three days of training was given. The structured questionnaire was discussed in detail, going through every question, and clarification was provided. A field manual was prepared for the supervisors and data collectors for use during data collection. The six data collectors were present in the respective hospitals during the complete 24 hours.

The data collectors collected the data daily. Medical record review and an interviewer-administered questionnaire were used to collect data on the intended variables of interest until the time of discharge from the hospital or 72 hours. We retained only the previously collected data were retained for analysis in cases of readmission. We assessed the neonates for the entire period of hospital stay (both in the maternity ward and neonatal intensive care unit). There was no follow-up after hospital discharge.

Data management and analysis

Early neonatal mortality was the event of interest, coded as “1” for failure and “0” for censored. Time-to-event was considered by subtracting the date of admission from the time of the event. Data entered into Epi-Data manager version 4.4 and analyzed using STATA™ version 16.0. for the follow-up time and age of the cohort, we calculated the mean and standard deviation. The cox-Proportional hazard model was used to determine risk factors for newborns’ survival time delivered at the hospitals. A tolerance level with a cut point of 0.2 was used to omit multicollinearity.

The Kaplan Meier curves were used to estimate survival time. The log-rank test was used to look at statistical variances between the groups of variables. Statistical significance was declared at $p\text{-value} < 0.05$. A summary statistic of proportions, including hazard ratio and 95% confidence intervals as used. Screening of risk factors for the newborn’s death was done employing bivariate Cox regression for each variable one at a period. Those variables with $p < 0.25$ throughout the bivariate Cox regression analysis were taken as an entrant variable for the multivariate Cox regression model to control possible confounders.

Ethics considerations

Ethical confirmation was granted from the Institution ethical Review Committee of Debre Tabor University, and all methods were performed following the relevant guidelines and regulations. A letter of formal permission and support was written to the respective administrator office. The aim of the research was undoubtedly clarified to concerned bodies. Mothers were told that they have the right to be involved or not to be involved in the study before they signed written informed consent. The research aims undoubtedly clarified, written informed consent-maintained, confidentiality ensured, and the study’s process explained to the neonates’ mothers. For mothers who were unable to read and write, data collectors read the respondents’ consent, and they mark if the respondents agree. The study participants were aware that data collectors were skilled only to gather evidence, and the data was not being passed to anybody. The confidentiality of the information (personal identification and idea were not used in a way that might threaten the respondent) was maintained, and the study participants’ privacy was respected. There was no payment/incentive for participating in this interview.

Operational definitions

Early neonatal mortality: This refers to a neonate’s death within the first 72 hours of life.

Neonatal survival: is referred to as being alive until the end of the follow-up period (72 hours).

Term pregnancy: is a pregnancy between 37 completed weeks up to 42 completed weeks of gestation.

Maternal First Delay: refers to the delay after the onset of real labour to reach a health facility.

Results

During the 72 hours' observation, 810 newborns (97.4% of the sample) followed for 37,454 new-borns-hours at the three hospitals. The mean ($\pm$ SD) length of stay at the four hospitals was 46.23($\pm$ 29.31) hours. Of the 810 newborns, 10.4% were stillbirths, 17.1% were alive but complicated, and 72.5% were alive without complications.

Maternal and neonatal clinical characteristics

Out of the 84 stillbirths, 25 were from among primiparous women, and 15 deaths in the first 72 hours out of the 38 deaths observed among women who gave 2 to 4 births. As Table 1 shows, 81.9% of the overall newborns survived were mothers who received antenatal care. Out of 84 stillbirths, 58 of them were diagnosed with intrauterine fetal death before starting real labour, whereas the rest 26 were fresh stillbirth during delivery (Table 1).

Table 1
New-borns and maternal clinical characteristics of Amhara regional state referral hospitals, Northern Ethiopia, 2018.

Variables	Categories	Still birth	Neonates died in the first 72 hours	Neonatas Survived
		Frequency(%)	Frequency(%)	Frequency(%)
Parity	One child	25(3.1)	13(1.6)	292(36.1)
	2 to 4 children	33(4.1)	15(1.8)	292(36.1)
	5 children and above	26(3.2)	10(1.2)	104(12.8)
Received Antenatal care	Yes	71(8.8)	35(4.3)	664(81.9)
	No	13(1.6)	3(.4)	24(2.9)
Place of delivery	Health institution	68(8.4)	31(3.8)	599(74.1)
	Home	15(1.8)	7(0.9)	88(10.9)
Newborn birth weight	< 2500	52(6.2)	31(3.8)	544(67.2)
	>=2500	32(3.9)	7(.8)	144(17.8)
APGAR score of the newborn	0–3	69(8.5)	7(0.8)	0(.0)
	4–6	2(0.3)	6(.7)	32(3.9)
	7–10	13(1.6)	25(3.1)	656(80.9)
Fetal outcome in the uterus	IUFD	58(7.2)	0(.0)	0(.0)
	NRFHR	14(1.7)	18(2.2)	184(22.7)
	RFHR	12(1.5)	20(2.5)	504(62.2)
Mode of delivery	Vaginal	33(4.1)	18(2.2)	340(41.9)
	Ceserean section (C/S)	51(6.3)	20(2.5)	348(42.9)
IUFD: intra-uterine fetal death, NRFH: non-reassuring fetal heart rate, RHFR:Reassuring fetal heart rate				

Neonatal illness

The leading cause of disease in Amhara regional state referral hospitals was neonatal jaundice 52(42.4%), followed by other complications 30(24.6%) like birth trauma, congenital anomalies, and asphyxia 22(17.7%) (Fig. 1).

Of the 688 newborns discharged, 56.7% were discharged alive, 2.5% were discharged with treatment, and 17.3% were referred to the neonatal intensive care unit (NICU). In contrast, the rest of the 23.5% were

discharged with an appointment.

Neonatal survival

During the study period, a total of 15.1% (n = 122) new-borns deaths were observed, making an overall newborn mortality rate of 151 per thousand births. Of the 122 newborn deaths, 84(68.9%) were stillbirths, 38(31.1%) died in the first 72 hours (Table 2). The overall incidence of new-borns mortality was 1.012 per thousand early neonate-hours.

Table 2
survival function life table of Amhara regional state referral hospitals, Northern Ethiopia, 2018

Time	Beg Total	Fail	Net Lost	Survivor Function	Std Error	[95% Conf. Int.]
1	810	82	0	0.8988	0.0106	0.8759 0.9176
6	728	0	117	0.8988	0.0106	0.8759 0.9176
12	611	0	2	0.8988	0.0106	0.8759 0.9176
20	609	1	1	0.8973	0.0107	0.8742 0.9163
24	607	15	95	0.8751	0.0119	0.8498 0.8964
48	497	6	68	0.8646	0.0125	0.8380 0.8871
50	423	1	0	0.8625	0.0126	0.8357 0.8853
52	422	1	0	0.8605	0.0127	0.8333 0.8835
72	421	16	405	0.8278	0.0146	0.7968 0.8544

Kaplan-Mair Survival Analysis

There was a higher mortality level in the first 24 hours compared to after 24 to 72 hours. This finding indicates a substantial reduction in death after the neonates survive the early 24 hours of life in the observation period (Fig. 2). Similarly, the curve indicates that neonatal mortality shows substantial decrement among those whose labour was monitored with Partograph (Fig. 3).

Determinants of neonatal mortality

We included the variables with a p-value of less than 0.25 in the crude model in the Cox proportional hazards regression model. Then, after controlling for potential confounders using multivariate Cox proportional hazard regression, the timing of first antenatal care visit, monitoring with partograph, type of admission of the women, and maternal complications within the first 24 hours (postpartum haemorrhage, fistula, and obstructed labour) were the variables that determine neonatal survival within the first 72 hours of life.

Gestational age at the first antenatal care visit was found to be a risk factor for newborn mortality. Women who came between 17 and 28 weeks of gestation for the first visit were 1.67 times more likely to lose their child [AHR = 1.67; 95% CI: 1.02, 2.73] compared to those who started the initial antenatal care visit before 16 weeks of gestation. Mothers not monitored with a partograph during labour were 2.66 times the risk of newborn mortality [AHR = 2.66; 95% CI: 1.70, 4.15] compared to their counterparts. Direct admission was 39% less risk of neonatal death than [AHR = 0.61; 95% CI: 0.38, 0.97] those admitted from referral to another health facility.

Maternal complications within 24 hours were also a significant risk factor for newborn mortality. Mothers experiencing postpartum haemorrhage were about three times risky for new-borns death [AHR = 2.88; 95% CI: 1.69, 4.89], and those who developed fistula in the first 24 hours were also about four times risky for new-borns death [AHR = 3.75; 95% CI: 1.23, 11.43]. Obstructed labor was more than twice risky [AHR = 2.14; 95% CI: 1.35, 3.38] for new-borns mortality and less than 1 hour maternal first delay in visiting health facility was 39% less risk of new-borns death [AHR = 0.61; 95% CI: 0.37, 0.98] (Table 3).

Table 3

Bivariate and Multivariate Cox-proportional hazard regression for the first three days neonatal mortality in Amhara regional state referral hospitals, Northern Ethiopia, 2018

Variables	Outcome		CHR (95%CI)	AHR (95%CI)
	Died	Censored		
Parity				
1 child	38(4.69)	292(36.05)	1.0	1.0
2–4 children	48(5.93)	292(36.05)	1.26[.82, 1.93]	1.20[0.74, 1.94]
5 children & above	36(4.44)	(104)12.84	2.25[1.43, 3.56] **	0.92 [0.52, 1.64]
Gestational age for the first antenatal care visit				
≤ 16 weeks	34(4.42)	343(44.55)	1.0	1.0
17 to 28 weeks	62(8.05)	307(39.87)	1.84[1.21, 2.80] *	1.67[1.02, 2.73] *
> 28 weeks	10(1.30)	14(1.82)	4.49[2.22, 9.10] **	1.21[0.51, 2.84]
Monitored with partograph				
Yes	63(7.78)	598(73.83)	1.0	1.0
No	59(7.28)	90(11.11)	4.48[3.13, 6.39] **	2.66[1.70, 4.15] **
Maternal mode of admission				
Direct admission	44(5.43)	437()	.37[.25, .53] **	0.61[0.38, 0.97] *
Referral	78(9.63)	251(30.99)	1.0	1.0
Mothers complications within 24 hours				
Abdominal distension	23(2.84)	68(8.40)	2.63[1.63, 4.26] **	1.24[.67, 2.32]
PPH	34(4.20)	38(4.69)	5.79[3.79, 83] **	2.88[1.69, 4.89] **
Fistula	5(0.62)	4(0.49)	6.59[2.64, 16.43] **	3.75[1.23, 11.43] *
No complication	60(7.41)	578(71.36)	1.0	1.0
Obstructed Labor				
Yes	74(9.14)	196(24.20)	2.78[1.93, 4.01] **	2.14[1.35, 3.38] *
No	48(5.93)	492(60.74)	1.0	1.0
Maternal first Delay				
< 1 hour	55(6.79)	560(69.14)	.25[.17, .36] **	0.61[0.37, 0.98] *

**p < 0.001, *p < 0.05, CHR- crude hazard ratio, AHR-adjusted hazard ratio and CI-confidence interval, the bold indicates significant variables

Variables	Outcome		CHR (95%CI)	AHR (95%CI)
	Died	Censored		
≥ 1 hour	67(8.27)	128(15.80)		1.0
**p < 0.001, *p < 0.05, CHR- crude hazard ratio, AHR-adjusted hazard ratio and CI-confidence interval, the bold indicates significant variables				

Discussion

Losing a newborn within the first three days of life, during which high neonatal mortality occurred, was shocking for the family, community at large and is devastating globally. Especially in developing countries, addressing this issue was difficult tasks for several factors. The study aimed to determine the incidence and determinants in the first three days among babies delivered in referral hospitals. In this study, 810 neonates born at the referral hospitals were included during the study period, and male predominance was noted in 53.5% of the study participants. This is in line with studies carried out in Pakistan (63%)[26], South Africa (57.8%)[27], in India (63.3%), in St Paul's Hospital Millennium Medical College (61.1%)[28] and University of Gondar hospital (58.3)[22], Ethiopia. Natural selection response to differential survival prospects [29] and cultural and social factors [22] was a discrepancy between female and male babies. Our study's causes of neonatal deaths were neonatal jaundice, complications such as birth trauma and congenital anomaly, asphyxia, umbilical sepsis, and neonatal sepsis, which are in line with the causes found in Ghana [30, 31], and Uganda [32].

In our study, 122 neonates were lost their lives within the first three days of life, giving an overall newborn mortality rate of 151/1000 total births, and the stillbirth rate was 103.7/1000 total births. This figure shows a significant decline from a study conducted in the Tikur Anbesa specialized hospital (225/1000 live births) [33], and (302/1000 live births)[22]. This decline might be due to the impacts of different interventions for the last six years. However, it was much higher than the global neonatal mortality rate in 2016 [34], and in studies conducted in Southern Ethiopia [35, 36], Eastern Ethiopia [37], Southwest Ethiopia [38], Sudan [39], Uganda [25], Zambia [40] and Ghana.[30] Our study is also much higher than a finding of a systematic review of PMR in Ethiopia that indicated 75/1000 live births at the institutional level, 43/1000 total births with follow up studies, 59.1/1000 total births in the Amhara region, and 29.5/1000 total births among early newborns (up to 7 days) [41]. The variances might be attributed to study designs, health service coverage, socioeconomic factors, and PMR's definition in other studies. The higher PMR in this study might also be because of the admission of complicated mothers and the consideration of PMR up to 3 days in referral hospitals. This finding implies that the situation of neonatal mortality is still not progressing as anticipated in referral hospitals and strengthen the argument made by the study conducted in Jimma Zone [38] and a previous systematic review [6], which concluded that "health facility delivery had no significant effect on neonatal mortality." However, this study's findings should be interpreted vigilantly because of the stillbirth rate reports among admitted term pregnant women in referral hospitals, and possible misclassification of pregnancy outcomes (e.g., severe asphyxia

of neonates) might overestimate the actual burden of stillbirth in the study area. Though there might be due to differences based on some factors, we suggest tailored and targeted interventions by all stakeholders at different levels.

Regarding the determinants of neonatal mortality within the first 72 hours, gestational age at the first antenatal care visit was a risk factor. Women who came between 17 and 28 weeks of gestation for the first visit were 1.67 times more likely to lose their child than those who started the initial antenatal care visit before 16 weeks of pregnancy. This finding is similar to studies conducted in Tigray regional state [42], Felege Hiwot referral hospital [43], and Gaza-Strip [44]. This result infers that the earlier the start of prenatal care visits, the more the mothers will have time to complete four follow-ups, which will help us a new method of obstetric problems, which suggests the recent WHO recommendation of positive pregnancy experiences [45]. Thus, this study suggests the early start of the antenatal visit and possible consideration of the new WHO recommendation for antenatal care visits in Ethiopian referral hospitals.

Maternal complications within 24 hours were also a significant risk factor for newborn mortality. Of these, the experience, postpartum haemorrhage, fistula development within the first 24 hours, and obstructed labour were found to be three times, four times, and more than twice risky for newborns death within the first 72 hours of life. Our study's findings regarding fistula and postpartum haemorrhage as risks for neonatal mortality were unique in this finding. The possible reason for neonatal mortality among mothers facing postpartum haemorrhage and fistula might be intrapartum asphyxia. In cases of maternal complications, the attention of health care providers diverts to saving the mother, and in some cases, neonates would not get adequate care, which leads them to intrapartum asphyxia. However, future research should be conducted to get the exact cause of neonatal mortality in such complications. However, this study's results, which identified obstructed labour as a risk of neonatal mortality, were similar to studies conducted in Hawassa University hospital, Ethiopia [46], and tertiary hospitals in Tanzania [47]. These findings might be due to asphyxia and other related consequences of prolonged labour leading to premature neonatal death.

Moreover, mothers who were not monitored with partograph during labour were nearly three times the risk of newborn mortality than their counterparts. This result was supported by a study in Addis Ababa [48] and Tigray regional state [42]. This outcome entails fetal-maternal health should be monitored with the start of the active first stage of labour for timely management of prolonged labour, and its consequences will be early identified as prevention and control of early neonatal death.

Furthermore, direct admission was 39% less risk of newborn mortality than those admitted from referral to another health facility. In other words, mothers who require a referral were either suffer from severe obstetric problems or transfer time. We extend the time to receive skilled care. Besides, less than one hour of maternal first delay to visit health was 39% less risk of newborn death. This result was similar to a study in Tigray Northern Ethiopia, showing that seeking skilled care at the start of labour was protective for perinatal mortality [42], Uganda [32], and India.[49] This result indicates that the first delay in maternal death also contributes to early neonatal death. We suggest that healthcare providers pay attention to

newborns' care with significant intrapartum asphyxia, including respiratory, temperature, and nutritional support.

Despite the indications of the Ghanaian study [30], this study has some inherent limitations. First, though this study was unique in addressing the first three days of life with a follow-up study design to determine the risk factors of early neonatal mortality, being only at the tertiary level of care may elevate the actual incidence estimate of premature neonatal death of the region. Second, the study was based on tertiary hospitals and may not show the picture of secondary and primary hospitals, and data were only collected up to 72 hours of the life of the newborns and, therefore, cases occurring after 72 hours were missed. Third, a mixed-method study design should have been used to identify the issues related to mothers and health care providers' perceptions of the quality of services provided in the referral hospitals. Further longitudinal studies focusing on early neonatal death should explore health system factors, maternal factors, and obstetric factors, especially in the first three days.

Conclusions

We hypothesized a high PMR in tertiary care centres in the first three days of life and found that about 1 in 7 newborns died in the first three days of life in the tertiary level of care in Northwestern Ethiopia. The leading causes of newborn death were neonatal jaundice, followed by complications, like birth trauma, congenital anomalies, and asphyxia.

Moreover, the determinants of PMR were delay for the first ANC visit, more than 1-hour maternal first delay to visit a health facility, and health system-related determinants such as not monitoring labour with, admission by referral were the significant factors. Furthermore, obstetric determinants were mothers' experience of postpartum haemorrhage, fistula development within the first 24 hours, and obstructed labour. Therefore, each hospital in the region must start implementing the WHO recommendation on positive pregnancy experience for addressing the health system and obstetric risk factors of newborn mortality. Additionally, awareness creation and adherence to the recommended level of care are essential.

Abbreviations

AHR
Adjusted Hazard Ratio; ANC:Antenatal Care, CHR:Crude Hazard Ratio; CI:Confidence Interval;
ETB:Ethiopian Birr; GA:Gestational Age; SD:Standard Deviation; WHO:World Health Organization

Declarations

Data Sharing Statement

The corresponding author will share the analyzed dataset upon request.

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Authors' contribution

All authors contributed to the work reported, whether in the conception, study design, execution, data acquisition, analysis, interpretation, or in all these areas. All authors also participated in drafting and revising or critically reviewing the manuscript. Finally, all of them gave final approval of the version to be published, have agreed on the journal to which the manuscript has been submitted, and agree to be accountable for all aspects of the work.

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Debre Tabor University covered the payment for data collectors and supervisors. However, the university had no role in study design, data collection, analyses, the decision to publish, and preparing the manuscript.

Availability of data and materials

The datasets generated during the current study are available from the corresponding author on a reasonable request.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

“Other complications” are birth trauma and congenital anomalies

Figure 1

New-borns morbidity in Amhara regional state referral hospitals, Northern Ethiopia, 2018 “Other complications” are birth trauma and congenital anomalies

Figure 2

K-M survival estimate of newborns in Amhara Regional state referral hospitals, Northern Ethiopia, 2018.

Figure 3

K-M survival estimate of neonates with labour monitored with partograph Amhara Regional state referral hospitals, North-west Ethiopia, 2018.

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