Proportion and factors of death among preterm neonates admitted in University of Gondar comprehensive specialized hospital neonatal intensive care unit, Northwest Ethiopia

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Abstract

Objective: Neonatal mortality accounts for 43% of under-five child mortality in Ethiopia where preterm is the second leading cause of neonatal death and steadily increased in low-income countries. Therefore, assessing the proportion of death and associated factors among preterm neonates has a paramount importance in designing an effective strategy to intervene and achieve sustainable development goal.

Results: In this study proportion of preterm neonatal death in this study was 28.8% [95% CI (25.1, 32.9)]. Complications during index pregnancy [AOR = 1.92, 95% CI (1.09, 3.38)], gestational age [AOR = 0.78, 95% CI (0.69, 0.91)], small for gestational age [AOR = 2.42, 95% CI (1.33, 4.38)], APGAR score at birth < 7 [AOR = 2.39, 95% CI (1.34, 4.27)], hyaline membrane disease [AOR = 5.15, 95% CI (2.83, 9.36)], neonatal respiratory distress at admission [AOR = 1.93, 95% CI (1.13, 3.31)], presence of jaundice [AOR = 3.39, 95% CI (1.90, 6.05)], received kangaroo mother care [AOR = 0.13, 95% CI (0.05, 0.35)], and hypoglycemia at admission [AOR = 3.86, 95% CI (2.12, 7.06)] were statistically significant. The proportion of preterm neonatal death was high. Ministry of health and responsible organizations should give special attention for preterm neonates to prevent life-threatening complications.

Keywords: Ethiopia, Preterm, Neonate, Death, Neonatal, Intensive care unit

Introduction

In the globe, approximately 3.1 million and 2.9 million neonatal deaths were reported in 2010 and 2014, respectively, which accounts 40% of the under 5 mortality. Despite a steady decline of neonatal mortality in African countries, it is not satisfactory [1, 2]. Globally, 3 in 4 neonatal deaths were caused by preterm birth complications which accounts for 35% of all neonatal deaths [3]. Infection (36%), preterm birth (28%) and birth asphyxia (23%) are the most common causes of neonatal mortality in the world [4–6].

Preterm (PT), a birth before 37 completed weeks of gestation, is the most frequent cause of neonatal death and the second leading cause of both neonatal and under-five mortality with multiple short and long-term health threats worldwide [7]. Lack of immunologic competence increases the risk of preterm infants for multiple infectious processes which may lead to long-term neurodevelopmental disorders and chronic lung disease [8].

 Ethiopian Demographic and Health Surveys reported that neonatal death was increased from 32% in 2005 to 43% in the 2016 and according to United Nations Children’s Fund (UNICEF) report, preterm birth which accounts 23% was believed to be a major and direct cause of neonatal death in Ethiopia [9, 10]. Causal factors linked to preterm birth are medical conditions of the mother or fetus, genetic influences, environmental exposure, infertility treatments, behavioral and socio-economic factors, medically indicated preterm delivery as well as iatrogenic prematurity [11, 12].

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Studies reported that preterm neonatal mortality ranged from 15 to 36% [1, 13, 14]. Reports from the world’s Low to Middle-income countries showed that 34 to 40% of neonatal mortality were contributed by preterm [5, 15–17]. Hospital-based studies in Africa reported that preterm neonatal mortality accounted for about 15.7 to 29.6% [18, 19]. Studies in Ethiopia reported that preterm neonatal mortality rate ranges from 18% up to more than 40% [20–26].

Different studies conducted so far showed that rural residency [18, 24], maternal age [27, 28], place of birth [20, 29], Obstetric risk factors were not having ANC [15–17], being prim para [4, 24], having any pregnancy complications [20, 29], Labour and delivery complications [15, 19, 23], having previous bad obstetrical history [16, 23] were risk factors for preterm neonatal death.

Neonatal related risk factors include being male sex [15–17, 30], low birth weight at birth [15, 24], gestational age (GA) at birth and neonatal congenital malformations [18, 23], neonatal clinical problems like respiratory distress syndrome (RDS), perinatal asphyxia (PNA), hyaline membrane disease (HMD), jaundice, hypoglycemia, hypothermia and neonatal sepsis [6, 23, 26, 31], timely initiation of breastfeeding upon birth and kangaroo mother care (KMC) were reported as factors of preterm neonatal death [26, 28].

Even if premature birth is not an acute disease, it is one of the major causes of infants’ death and preterm birth continues to be significant public health problem by increasing the average cost of medical care for a premature and low birth-weight baby for the first year of life for developing country like Ethiopia. These high medical expenses could burden both the parents, families as well as the community. Therefore, this is the dual agenda to prevent preterm birth and reduce neonatal death which requires a comprehensive research strategy to end the preventable deaths of newborns and under-five children.

Main text
Methodology

Study design and setting
Retrospective cross-sectional study was conducted to assess the proportion of death and its associated factors among preterm neonates admitted in NICU from January 2016 to March 2018 in University of Gondar comprehensive specialized hospital neonatal intensive care unit. The hospital is one of the largest teaching hospital found in Amhara region providing tertiary level care for more than seven million people in the North West part of the country.

Sample size and sampling procedure
All preterm neonates admitted to neonatal intensive care unit at the University of Gondar comprehensive specialized hospital. Thus, preterm neonates admitted to NICU with a gestational age of less than 37 completed weeks were source population and all preterm neonates who were admitted to neonatal intensive care unit (NICU) at University of Gondar comprehensive specialized hospital from January 2016 to March 2018 were the study population. A total of 516 preterm neonates admitted in NICU were included in the study.

Data collection method and instruments
Medical records were reviewed and preterm neonatal cards were identified by their medical registration/card number. Then data were extracted using structured and pretested data extraction checklist prepared in English from HMIS registration format and patients’ card. Trained midwife professionals had collected the data.

Data quality assurance and analysis
Data were entered into EPI info version 7 and imported to Stata version 14 statistical software for further analysis. Descriptive statistical data analysis was done and followed by bivariate and multivariable analysis in order to see the statistical association between the outcome and explanatory variables. Variables which showed significant association in the bivariate analysis were entered into multivariable logistic regression. The degree of association was assessed using odds ratio with 95% confidence interval and P-value < 0.05 were taken as statically significant.

Results
Socio-demographic and obstetric characteristics of mothers
In this study, 516 preterm neonates’ data were included in the analysis. Two-third (66.86%) of the mothers were resided out of Gondar town. About one-fifth 417 (80.81%) of mothers were in the age range of 20–34 years with mean age of 26.52 years (Table 1).

Characteristics of the preterm neonates
Among 516 preterm neonates, 303 (58.73%) were males and 109 (21.12%) were small for gestational age. About one-sixth 82 (15.89%) had a body temperature of greater or equal to 36 °C measured within 1 h of admission and 371 (71.9%) were heated under radiant warmer. (Table 2).

Proportion of preterm neonatal death
This finding showed that 149 (28.8%) with 95% CI; (25.1, 32.9) neonates died. From this 17 (11.4%) of them...
were died within the first 24 h of life and 127 (85.23%)
died in the first 7 days of life (early neonatal death). The
causes of death were multifactorial, not single. How-
ever, the leading causes were PNA (31%), HMD (26%),
and cardiorespiratory arrest due to apnea (17%).

### Table 1 Socio-demographic and obstetric characteristics
of mothers of preterm neonates admitted in NICU at
University of Gondar comprehensive specialized
Hospital from January 2016 to March 2018 (n = 516)

| Characteristics                        | Frequency | Percent |
|----------------------------------------|-----------|---------|
| Maternal residence                     |           |         |
| Gondar town                            | 171       | 33.14   |
| Out of Gondar town                     | 345       | 66.86   |
| Age of women in years                  |           |         |
| < 20                                   | 41        | 7.95    |
| 20–34                                  | 417       | 80.81   |
| ≥ 35                                   | 58        | 11.24   |
| Had ANC in index pregnancy             |           |         |
| Yes                                    | 486       | 94.2    |
| No                                     | 30        | 5.8     |
| Parity (Number of births)              |           |         |
| I                                      | 230       | 44.57   |
| II–IV                                  | 196       | 37.99   |
| ≥ V                                    | 90        | 17.44   |
| Complication during index pregnancy    |           |         |
| Yes                                    | 120       | 23.26   |
| No                                     | 396       | 76.74   |
| Previous bad obstetrics history        |           |         |
| Yes                                    | 80        | 15.5    |
| No                                     | 436       | 84.5    |
| Type of pregnancy                      |           |         |
| Singleton                              | 331       | 64.15   |
| Multiple                               | 185       | 35.85   |
| Onset of labor                         |           |         |
| Elective caesarean section             | 56        | 10.85   |
| Spontaneous                            | 425       | 82.37   |
| Induced                                | 35        | 6.78    |
| Place of birth                         |           |         |
| Home                                   | 23        | 4.50    |
| Health center                          | 120       | 23.25   |
| Hospital                               | 373       | 72.25   |
| Mode of delivery                       |           |         |
| Spontaneous vaginal delivery           | 384       | 74.42   |
| Caesarean section                      | 117       | 22.67   |
| Instrument assisted delivery           | 15        | 2.91    |
| Duration of labour in hours (n = 460)  |           |         |
| < 4                                    | 52        | 11.30   |
| 4–18                                   | 354       | 77.00   |
| > 18                                   | 54        | 11.70   |

### Associated factors of proportions of death for preterm neonates

Univariate and multivariable logistic regression was
used to identify associated factors of death for preterm neonates admitted in the NICU.

Findings from bivariate analysis showed that compli-
cations during index pregnancy, previous bad obstetric
history, neonatal respiratory distress, gestational age,
small for gestational age, low APGAR score at birth,
HMD, PNA, jaundice, receiving KMC, hypoglycemia,
hypothermia, and temperature within 1 h of admission
in °C were significantly associated with death of pre-
term neonates.

However, in the multi-variable analysis complications
during the index pregnancy, neonatal respiratory distress,
gestational age, small for gestational age, low APGAR
score at birth, HMD, jaundice, receiving KMC, and hypo-
glycemia remained statistically significant factors.

The odds of death among preterm neonates delivered
from mothers having complication during index preg-
nancy was 1.92 times higher as compared to their coun-
terparts [AOR = 1.92; 95% CI (1.09, 3.38)].

The odds of death for preterm neonates who had < APGAR score at birth was 2.4 times higher than those who had > APGAR score at birth [AOR = 2.39; 95%
CI (1.34, 4.27)].

Providing KMC for all preterm neonates reduce the
odds of death by 87% as compared to not provided KMC
[AOR = 0.13; 95% CI (0.05, 0.35)] (Table 3).

### Discussion

The proportion of death among preterm neonates admitted in University of Gondar Comprehensive Specialized Hospital NICU was 28.8% [95% CI (25.1, 32.9)]. The causes of death weren't single problem rather combina-
tion of problems lead to death and the major once were PNA, HMD, jaundice, clinical sepsis and cardiorespira-
tory arrest due to apnea. All the causes are preventable by improving timely health seeking behavior of the com-
munity, upgrading the quality of care provided in the hospitals and health centers to be safe, clean and well
equipped with all the infrastructures. This finding is in line with studies conducted in a multi-country level analysis reported by WHO and UNICEF 29.3% [14] and in Kenya 29.6% [19]. However, this finding was higher than studies conducted in a multi-country analysis by the lead of saving the children 15% [13] Cameroon 15.7% [18] Jimma Ethiopia 18.2% [20] and northern rural Ethiopia 23.7% [21].

This might be due to the difference in the study setting and the study population which was most vulnerable pre-
term neonates only.
In contrast, this finding was lower than studies conducted in population-based study from low to middle-income countries 37.5% [15], Urban Pakistan 34% [5], Jordan 40% [16], Johannesburg South Africa 64% [17], Tigray region Northern Ethiopia 34% [22–24] and Jimma University Specialized Hospital, Ethiopia 34.9% [26]. This might be due to the time variation where neonatal mortality is decreasing, access of health care service was increased, the health seeking and utilization behavior of the community and accessibility of trained health care providers are comparatively increased.

This finding showed that a neonate delivered from mothers with Complication during index pregnancy increased the odds of death by 92% as compared with their counterpart [AOR $= 1.92$, 95% CI (1.09, 3.38)]. This finding was supported by findings in northern Ethiopia [24], Ethiopian, DHS data [28], the sub-urban hospitals of Cameroon [18] and Johannesburg Central Hospital [29]. This similarity might be due to the complications (PROM, PIH, and delivery complications) affecting the pregnancy to result in preterm labour and acquired infections leading to neonatal death.

In this study, as the gestational age increase in a week, the odds of death was decreased by 22% [AOR of 0.78; 95% CI (0.69, 0.91)]. This finding was in line with findings in Jimma University specialized hospital [26] and Addis Ababa St. Paul’s Hospital Millennium Medical College [25]. This was because, as gestational age increases fetal maturity will be maximized and risk of life-threatening complications associated with prematurity may decrease.

This study showed that a neonate with small for gestational age at birth was 2.42 times at higher risk of death compared to appropriate for gestational age [AOR $= 2.42$, 95% CI (1.33, 4.38)]. This finding was supported by a study conducted in Jimma Zone [20] Ethiopian, DHS data [27], and Johannesburg Central Hospital [29]. The possible reasons might be due to that if small for gestational age the occurrence of life-threatening complications which lead to death is high compared to appropriate for gestational age neonates.

The odds of death was increased by 2.4 times for a neonate with APGAR score < 7 at birth as compared to the

| Characteristics | Frequency | Percent |
|-----------------|-----------|---------|
| Sex of the neonate | Male 303 | 58.73 |
| | Female 213 | 41.27 |
| Gestational age (weeks) | < 32 107 | 20.74 |
| | 32–35 269 | 52.13 |
| | 35–37 140 | 27.13 |
| Weight for gestational age at birth | Small 109 | 21.12 |
| | Appropriate 407 | 78.88 |
| Newborn cry immediately at birth | Yes 385 | 74.61 |
| | No 131 | 25.39 |
| Bag and mask resuscitation at birth | Yes 209 | 40.5 |
| | No 307 | 59.5 |
| Newborns temperature with in 1 h of admission | ≤ 32 15 | 2.91 |
| | 32.1–34 151 | 29.26 |
| | 34.1–35 158 | 30.62 |
| | 35.1–36 110 | 21.32 |
| | ≥ 36 82 | 15.89 |
| Peri-natal asphyxia diagnosed at birth | Yes 137 | 26.55 |
| | No 379 | 73.45 |
| Newborn diagnosed with respiratory distress | Yes 142 | 27.52 |
| | No 374 | 72.48 |
| Hypothermia diagnosed at admission | Yes 426 | 82.56 |
| | No 90 | 17.44 |
| Hypoglycemia diagnosed at admission | Yes 112 | 21.71 |
| | No 404 | 78.29 |
| Jaundice | Yes 127 | 24.61 |
| | No 389 | 75.39 |
| Newborn diagnosed with clinical sepsis | Yes 401 | 77.71 |
| | No 115 | 22.29 |
| Neonate received photo therapy | Yes 143 | 27.71 |
| | No 373 | 72.29 |
| Neonate received continuous positive airway pressure | Yes 287 | 55.62 |
| | No 229 | 44.38 |
In the current study, the odds of preterm neonatal death among cases of HMD was 5 times higher compared to none cases [AOR = 5.15, 95% CI (2.83, 9.36)]. This finding was comparable with findings in Jimma University specialized hospital [26] and Johannesburg Central Hospital [29]. This might be HMD is a disease of prematurity affecting respiratory function leading to death in preterm neonates.

The odds of death for preterm neonates with respiratory distress was 1.9 times higher than their counterparts [AOR = 1.93, 95% CI (1.13, 3.31)]. This finding was in line with findings in Butajira District, South Central Ethiopia [6], and Jimma University specialized hospital [26]. Because it is life-threatening complication leading to hypoxic-ischemic encephalopathy.

Preterm neonates with jaundice had 3.4 times higher odds of death than their counterparts [AOR = 3.39, 95% CI (1.90, 6.05)]. This finding was in line with findings in Jimma University specialized hospital [26]. This might be due to that gastrointestinal immaturity, liver enzyme deficiency leading to excess production of bilirubin to result in brain toxicity and death.

Hypoglycemia was significantly associated with the odds of death for preterm neonates, [AOR = 3.86, 95% CI (2.12, 7.06)]. This might be because of luck of adipose fat tissue serving as a source of glucose to adapt the extrauterine life until they maintain through feeding.

This finding showed that the odds of death among preterm neonates received KMC was lowered by 87% [AHR = 0.13, 95% CI (0.05, 0.35)]. This might be KMC prevents hypothermia by reducing body surface area to the external environment and helps easily accessing breastfeed on demand.

### Conclusions

In this study the proportion of preterm neonatal death was high. Complications during the index pregnancy, respiratory distress, gestational age, small for gestational age, low APGAR score at birth, HMD, jaundice, receiving KMC, and hypoglycemia were found to be significant factors for preterm neonatal death. All responsible bodies should work on quality care at ANC to maximize maternal health conditions, access NICU with infrastructures and skilled manpower at health institutions and give special care for preterm to avoid complications due to preterm.

### Limitation

It was a cross-sectional study and may not show the cause and effect relationship. A secondary source of data may lack some important variables affecting the outcome variables.
Abbreviations
ANC: antenatal care; AOR: adjusted odds ratio; APGAR: Appearance Pulse Grimace Activity Respiration; ARH: antepartum hemorrhage; B.Sc.: Bachelors of Science; CI: confidence interval; COR: crude odds ratio; EDHS: Ethiopian Demographic and Health Survey; GA: gestational age; HIV: human immunodeficiency virus; HMD: hyaline membrane disease; HR: hazard ratio; IRB: Institutional Review Board; KMC: kangaroo mother care; NEC: necrotizing enterocolitis; NCPAP: nasal continuous positive air pressure; NICU: neonatal intensive care unit; NGOs: non-governmental organizations; NMR: neonatal mortality rate; OR: odds ratio; PIH: pregnancy induced hypertension; PNA: perinatal asphyxia; PROM: prelabour rupture of membrane; PT: preterm; RDS: respiratory distress syndrome; UN: United Nations; UNICEF: United Nations International Emergency Children Fund; WHO: World Health Organization.

Authors’ contributions
AEY conceived and design the idea, participated in the data collection process, analyze data and wrote the paper. AAT participated in data analysis and wrote the paper. Both authors read and approved the final manuscript.

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Competing interests
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Availability of data and materials
Data will be available upon responsible request from the corresponding author using “ayenewe07@gmail.com”.

Consent for publication
Not applicable.

Ethics approval and consent to participate
Ethical approval was obtained from the Institutional Review Board (IRB) of the Institute of Public Health, College of Medicine and Health Science University of Gondar. Permission letter from University Hospital was also secured before data collection. Names of patients were not included during data collection.

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