

# Causes of Neonatal Death in Ayder Comprehensive Specialized Hospital, Ethiopia

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## ABSTRACT

**Background:** The first 28 days of life are the most sensitive time regarding a child's survival and health. Neonatal death accounts for a major part of under-five deaths, especially in sub-Saharan Africa. In this regard, the present study aimed to identify the causes of neonatal deaths in Ayder Comprehensive Specialized Hospital, Tigray, Ethiopia.

**Methods:** The present institution-based descriptive cross-sectional study was conducted on neonates admitted to the neonatal intensive care unit of Ayder Comprehensive Specialized Hospital from June 2018 to May 2019. The required data were extracted from the medical charts of the patients during admission and discharge and their death certificates. The collected data were analyzed in SPSS software (version 23) using descriptive statistics to describe the prevalence and causes of neonatal deaths. The final results were summarized using frequencies and proportions.

**Results:** In total, 1785 neonates were admitted during the study period and 1388 (77.8%), 99 (5.5%), and 298 (167 per 1000 live births) of them were treated and discharged, discharged against medical advice, and died, respectively. The causes of 139 (46.6%), 72 (24.2%), 63 (21.1%), and 22 (7.4%) neonatal deaths in the hospital were prematurity-related complications, neonatal sepsis, perinatal asphyxia, and congenital anomalies, respectively. The highest mortality rate was observed in neonates with respiratory distress syndrome since 89 out of 127 (70.8%) afflicted neonates died. Moreover, the second-highest mortality rate was found in newborns with perinatal asphyxia as 63 out of 174 (36.2%) afflicted newborns died. Furthermore, it was found that almost all deaths (98.3%) occurred during the first seven days after birth.

**Conclusion:** Based on the results, it can be concluded that the neonatal mortality rate was substantially high among the studied neonates. Moreover, the case fatality rate of respiratory distress syndrome was alarmingly high. Therefore, all the people who are in charge must devote a considerable effort to improve the health care delivered to neonates.

**Keywords:** Ayder comprehensive specialized hospital, Causes, Death, Descriptive cross-sectional, Neonate

## Introduction

The neonatal period is defined as the first 28 days of life and can be categorized into the very early (first 24 h), early (first 7 days), and late neonatal (7-28 days) periods (1). Newborn health has an increasingly significant role in the Sustainable Development Goals. In this regard, it must be noted that the first day and the first 28 days of life are the most sensitive time for a child's survival and health (2).

Based on the statistics, 2.5 million infants died worldwide in the first month after birth in 2018 and approximately 7,000 neonates died per day with about one third dying in the first 24 h of life

and about 75% dying in the first seven days after birth. Moreover, the rate of neonatal death decreased more slowly, compared to that of children aged 1-59 months. Consequently, the share of neonatal deaths among all under-five mortalities increased to 40% and 47% in 1990 and 2018, respectively. More specifically, 75% of neonatal deaths result from prematurity, complications during labor and delivery, and neonatal infections.

According to the statistics, Sub-Saharan Africa had the highest neonatal mortality rate in 2018 which was 28 deaths per 1,000 live births,

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followed by Central and Southern Asia with 25 deaths per 1,000 live births. A child born in sub-Saharan Africa or Southern Asia is 10 times more likely to die in the first month than a child born in a high-income country (3). Out of the 10 countries with the highest newborn mortality rates, 8 were in Sub-Saharan Africa and 2 in South Asia. Ethiopia ranks fifth in this list and had the highest rate of newborn death in 2016 (90 per 1,000) (4).

Based on the statistics, neonates born to poor families are 1.4 times more likely to die during the first 28 days, compared to those born to richer families (5). Despite this significant rate of neonatal death, there are few studies performed on the causes of such deaths in Tigray. Moreover, based on the review of the related literature, no similar study had been conducted in the selected hospital. Therefore, this study aimed to assess the causes of neonatal deaths in Ayder Comprehensive Specialized Hospital (ACSH).

## Methods

The present study was conducted in ACSH, located in the Tigray region in Mekelle town, which is 778 km from the capital city, Addis Ababa. It started as a referral and specialized medical center in 2008 and now delivers clinical services to more than 8 million people in its catchment area which includes Tigray, Afar, and South-eastern parts of the Amhara regional state.

This hospital provides a broad range of medical services, including both inpatient and outpatient care to all age ranges. It also serves as a teaching hospital for medical and other health sciences in both undergraduate and postgraduate programs. The Pediatrics and Child Health Department provides services at the outpatient clinics, emergency department, wards for under and above-five children, pediatric intensive care units, and neonatal intensive care unit (NICU). The NICU provides services for approximately 200 neonates per month with a total of 43 beds and one room for Kangaroo mother care. There are 65 nurses, 1 neonatologist, 1 general pediatrician, 4 residents, and 8 interns. This hospital is equipped with four radiant warmers, six incubators, five phototherapies, one mechanical ventilator, and one x-ray machine.

## Study Design

This institution-based descriptive cross-sectional study was conducted on neonates admitted to the NICU in ACSH during June 2018-May 2019. It should be noted that all the neonates who were admitted to the NICU during the

forementioned period were included in the study. However, those neonates who were kept in the hospital for further examinations or their medical charts were incomplete were excluded from the study.

The required information was collected in the form of semi-structured data that were gathered by trained medical interns working in the NICU. The study variables consisted of gestational age, birth weight, mode and place of delivery, diagnosis, outcome, and laboratory data. The diagnosis and causes of death of specific disease were determined by experienced physicians (residents, pediatricians, and a neonatologist).

## Statistical analysis

The collected data were checked, cleaned, and entered into SPSS software (version 23) using the descriptive analysis, such as frequency distribution and tables.

## Ethical consideration

Ethical clearance was obtained from the Institutional Review Board (Health Research Ethics Review Committee) of the College of Health Sciences of Mekelle University. Moreover, permission was obtained from ACSH medical directors and a support letter was also acquired from the chief clinical director. Furthermore, the collected data were kept confidential and not used for purposes other than those of the present study. However, the consent of the patients was not needed for this medical chart review study since the college reserves the right to own the medical charts of the patients.

## Operational definition

In the present study, the gestational age was calculated based on the last menstrual period of the mother (LMP); however, if she did not know her LMP, it was estimated using the new Ballard score. This score was used to estimate the gestational age of those neonates who were less than 72 h of age. Moreover, the neonates born before 37 completed weeks of gestation were considered premature (6).

In this research, the diagnosis of neonatal disease was mainly made clinically with a detailed history and physical examination, supported by necessary laboratory investigations, such as complete blood count, chest X-ray, blood culture, and, if needed, imaging (e.g., magnetic resonance imaging). Nevertheless, sometimes the diagnosis of neonatal sepsis was made based on the clinical signs of possible serious bacterial infection which

were provided by WHO's Integrated Management of Childhood Illness guidelines. These signs included a history of difficulty feeding, history of convulsions, the movement only when stimulated, respiratory rate of 60 or more breaths per min, severe chest retractions, or a temperature of  $>37.5^{\circ}\text{C}$  or  $<35.5^{\circ}\text{C}$  (7).

Neonates whose sepsis was diagnosed within the first 72 h after the birth were labeled as having the early-onset neonatal sepsis, while those whose sepsis was diagnosed after 72 h of life were labeled as having late-onset neonatal sepsis.

The diagnosis of respiratory distress syndrome (RDS) was made when a neonate was born preterm and had clinical signs of rapid breathing, cyanosis, grunting, chest indrawing, decreased air entry bilaterally to the lung fields, low saturation of oxygen with pulse oximetry, chest X-ray examination with signs of RDS, and immediate symptoms after birth (8).

Meconium aspiration syndrome was diagnosed based on respiratory distress (manifesting as tachypnea, cyanosis, and air trapping, together with reduced pulmonary compliance) in a neonate born in meconium-stained amniotic fluid whose symptoms could not be explained by other causes. In this case, the chest typically appears barrel-shaped, with an increased anterior-posterior diameter due to over inflation. Moreover, rales and rhonchi are heard during auscultation usually shortly after birth (9). Furthermore, in the present research, perinatal asphyxia was diagnosed if the 5th APGAR score was less than 7.

The definitions provided by WHO were used

for prematurity, low birth weight (LBW), very low birth weight, extremely low birth weight, and congenital malformations (body deformity or birth defects which were believed to have an impact on the health of the baby) (10). Furthermore, the anthropometry was interpreted using the Lubchenco curve (11).

Neonatal Mortality Rate refers to the number of deaths in the first 28 days of age per 1000 live births. In the present research, it was not possible to do pathologic and autopsy examinations to confirm the cause of death.

## Results

A total of 1785 newborns were admitted during the study period. The majority of the neonates ( $n=1069$ , 60%) were male and the male to female ratio was 1.5:1. Moreover, eight neonates (0.4 %) had a disorder of gender development. More than half of the admitted neonates ( $n=918$ , 51.4%) were born in ACSH, while the others were outborn (Table 1).

### *Clinical characteristics of the studied neonates*

In total, two-third of the studied neonates were admitted within the first 24 h of life while 7.4% of them were admitted within the first seven days of life. Moreover, 615 (34.4%) of them were diagnosed with neonatal sepsis among which 488 (79.3%) and 127 (20.7%) were admitted with early- and late-onset of sepsis, respectively.

Furthermore, 431(24.1%), 196 (11%), and 268 (15%) of the neonates were admitted due to prematurity, perinatal asphyxia, and hyperbilirubinemia, respectively. A total of 197 (11%)

**Table 1.** Socio-Demographic and Clinical Characteristics of Neonates Admitted to Ayder Comprehensive Specialized Hospital from June 2018 to May 2019 (N=1785)

Variables	Female	Male	DGD	Total (%)
Place of residence				
Urban	428	630	5	1063 (59.60)
Rural	280	439	3	722 (40.40)
Gestational age				
Less than 37 weeks	183	244	4	431 (24.30)
37-42 weeks	501	789	4	1294 (73.10)
More than 42 weeks	15	31	0	46 (2.60)
Place of delivery				
Inborn (in ACSH)	332	531	4	867 (48.60)
Outborn (both outside of ACSH and home)	377	531	4	918 (51.40)
Birth weight				
<2500 gram	270	336	4	599 (34.70)
2500-3999 gram	402	660	4	1066 (61.70)
>4000 gram	23	39	0	62 (3.50)
Anthropometry				
AGA	543	839	7	1397 (85.60)
SGA (term)	82	102	1	176 (10.80)
LGA	20	38	0	58 (3.60)
Not applicable	65	90	0	154 (8.60)

AGA: appropriate for gestational age; SGA: small for gestational age; LGA: large for gestational age; DGD: disorder of gender development; ACSH: Ayder Comprehensive Specialized Hospital

**Table 2.** Major causes of deaths of neonates admitted to Ayder Comprehensive Specialized Hospital from June 2018 to May 2019 (n=298)

Causes	Number of Deaths (percent)	Case fatality rate
Prematurity (n=431)	139 (46.6%)	32.25%
RDS (n=127)	89 (29.9%)	70.80%
Sepsis(n=183)	27 (9.09%)	6.26%
Asphyxia(n=22)	15 (5%)	3.40%
With Jaundice( n=63)	9 (3%)	2.00%
Neonatal sepsis (n=432)	72 (24.1%)	16.70%
Perinatal asphyxia (n=174)	63 (21.1%)	36.20%
Congenital anomaly(n=190)	22 (7.4%)	11.60%
Others (n=353)	2 (0.67%)	0.56%

RDS: respiratory distress syndrome

**Table 3.** Outcome of neonates admitted to Ayder Comprehensive Specialized Hospital

	Number	Percent
Treated and discharged	1388	77.8
Discharged against medical advice	99	5.5
Death	298	16.7

neonates were admitted with congenital anomalies, 93 (47%), 21 (1.2%), 15 (0.8%), and 25 (1.4%) of which were meningocele/myelomeningocele, congenital heart disease, clubfoot, and trisomy, respectively.

### **Causes of neonatal deaths in Ayder Comprehensive Specialized Hospital**

The three common causes of neonatal deaths in this study were prematurity-related complications, neonatal sepsis, and perinatal asphyxia which accounted for 139 (46.6%), 72 (24.2%), and 63/298 (21.1%) deaths, respectively. The RDS with a case fatality rate of 70.8% was the most common cause of preterm mortality (Table 2).

### **Outcome of neonates admitted to Ayder Comprehensive Specialized Hospital**

More than three-fourths of all the admitted neonates (n=1388, 77.8%) were treated and discharged, while 99 (5.5%) of them were discharged against medical advice and 298 (16.7%) of them died. Majority of the neonates who died (n=186, 62.4%) were male.

### **Age of neonates at the time of death**

Nearly one-third of the neonates died in the first 24 h after birth while 77% of them died in the first 72 h of life. Almost all the deaths (98.3%) happened during the first 7 days of neonatal age.

## **Discussion**

Given the high mortality rate of the neonates in ACSH, the present study aimed to identify the causes of neonatal deaths in this hospital. In the present study, the overall neonatal mortality rate

was 16.7% which was similar to the results of the studies conducted in Nigeria, Ghana, and Military Hospital, Kharian, Pakistan (12,13,14). However, this mortality rate was lower than those of the Mizan-Tepi Teaching Hospital, Ethiopia and St. Paul's Hospital, Addis Ababa (14,15) and higher than those of the University of Gondar Hospital, Felege HIWOT Referral Hospital, and the teaching hospital of Uttarakhand in India (16,17,18,19).

This significant discrepancy in the death rate of different hospitals may be due to the differences in their health care services, the level of the skill of the staff, and also the difference in their methodology. Nevertheless, it should be noticed that the death rate could have been even higher if it was possible to know the final outcome of the neonates who were discharged against medical advice (n=99, 5.5%).

Based on the results, the mortality rate in male neonates (62.4%) was higher in comparison to the female neonates. This is consistent with the findings of a study performed in South Africa where 63% of the deaths were observed in male neonates (20). The reason could be the fact that boys are biologically weaker and more vulnerable to illness and early death due to differences in the biology and genetic makeup of the two genders (21).

The three common causes of neonatal mortality in this study were prematurity-related complications, neonatal sepsis, and perinatal asphyxia. In total, 46.6% of death in the present study were due to prematurity-related complications. This is comparable to the results of the studies carried out in north-central Nigeria, Ghana, and South Africa in which 43.2% (22), 44.8% (13), and 43% of deaths were due to

prematurity-related complications (20).

Based on the results, neonatal sepsis accounted for 24.2% of the neonatal deaths in this research which is consistent with the findings of a study conducted in Kermanshah, Iran in which 22.6% of neonatal deaths were secondary to neonatal sepsis (23). The rate of neonatal infection in low resource countries is higher, compared to the developed countries which could be due to their low socioeconomic status and the presence of other risk factors, such as prematurity, LBW, prolonged labor, and rupture of membranes (24).

Perinatal asphyxia also accounted for 21.1% of the deaths in the present study. This is consistent with the results of a study carried out in Pakistan, in which 20.8% of the deaths were due to perinatal asphyxia (25). This may suggest that there are problems and inadequacies in the care provided for women in labor and resuscitation of the neonates.

The case fatality rate of prematurity-related complications in this study was 32.25% which is higher than that of a study conducted in Nigeria (27.8%) (26) and lower than that of a study performed in India (46.9%) (27). These variations could be due to the difference in the availability of the equipment in health facilities (mechanical ventilator and surfactant). It should be noted that among the prematurity-related complications, the case fatality rate of RDS was alarmingly high (70.8%).

The case fatality rate of perinatal asphyxia in this research was 36.2% which is in line with that of a study carried out in Karachi, Pakistan (36%) (28). However, this rate was lower than that of the hospital in Rawalpindi (43.8%) (29) and higher than that of the studies conducted in Nigeria (27.6%) (26) and Bangladesh (22%) (30). Proper antenatal and intrapartum follow-up of high-risk pregnant mothers, on-time referral to the hospital, and newborn resuscitation at the time of birth should be mandatory at all health facilities to decrease the high case fatality rate of birth asphyxia.

The case fatality rate of neonatal sepsis was 16.7% in the present study which is in line with that of a study performed in Military Hospital in Kharian (15.22%) (14). However, this rate in ACSH was higher than that of the hospital in Rawalpindi (12.5%) (29) and lower than those of the hospitals in Karachi, Pakistan (30.75%) (28) and India (34.4%) (27). This could indicate that there are differences in the infection prevention practices in the neonatal units and delivery rooms

of different hospitals. Moreover, this discrepancy could also be explained by the difference in the quality of care delivered in different health facilities.

The highest mortality rate was observed in the first week of life since 98.3% of neonates died during this period. This is consistent with a study conducted at Mizan-Tepi University Teaching Hospital where 97.7% of neonatal deaths occurred in the first 7 days of life (15). However, this is higher than the reported mortality rate of this period by WHO (3). The high mortality rate in the first seven days of life might be due to the high prevalence of deaths secondary to RDS.

Therefore, it is clear that the majority of neonatal deaths can be prevented by the identification of the high-risk pregnant mothers, provision of proper and timely obstetrical care, and intensification of the neonatal care.

### **Strengths of the study**

This was the first study conducted on the prevalence and causes of neonatal mortality in the ACSH. It must be noted that neonates were included from both rural and urban areas of residence.

### **Limitations**

One of the limitations of the study was its retrospective design. Moreover, a significant number of medical charts were incomplete and it was not possible to perform an autopsy examination to find out the specific causes of death.

### **Conclusion**

Based on the results, the neonatal mortality rate was high in the ACSH hospital. Moreover, it can be concluded that almost all of the neonatal deaths occurred in the first 7 days of life and that prematurity, neonatal sepsis, and perinatal asphyxia were the common causes of mortality, in that order. In addition, it was found that the case fatality rate of RDS was alarmingly high (70.8%).

It is suggested that regular antenatal follow-up be provided for pregnant mothers and their partograph be recorded as well. The physicians working at the NICU must make a significant effort to diagnose diseases early and initiate the appropriate treatment for the admitted neonates. In addition, nurses should provide appropriate continuous nursing care.

### **Data sharing statement**

All important data are included in the

manuscript.

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None.

## Conflicts of interest

None.

## References

- Carlo WA. Overview of mortality and morbidity. Kleigman RM, Stanton BF, Geme III JW, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics. 20<sup>th</sup> ed. Philadelphia: WB Saunders; 2016. P. 789.
- World Health Organization. Reaching the every newborn national 2020 milestones: country progress, plans and moving forward. Geneva: World Health Organization; 2017.
- World Health Organization. Newborns: reducing mortality. Geneva: World Health Organization; 2019.
- UNICEF. The World Bank, the United Nations population division: levels & trends in child mortality: estimates developed by the UN Inter-agency group for child mortality estimation. New York, USA: IGME; 2012.
- UNICEF. Committing to child survival: a promise renewed; progress report 2014. New York: UNICEF; 2014.
- Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard score, expanded to include extremely premature infants. *J Pediatr*. 1991; 119(3):417-23.
- Fuchsa A, Bielickia J, Mathur S, Sharlan M, Johannes N. Antibiotic use for sepsis in neonates and children evidence update. Washington, DC: WHO Reviews; 2016.
- Martin RJ, Fanaroff AA, Walsh MC. Respiratory distress in the neonate. Fanaroff and Martin's neonatal-perinatal medicine e-book: diseases of the fetus and infant. 10<sup>th</sup> ed. Amsterdam, Netherlands: Elsevier Health Sciences; 2015.
- Fanaroff AA. Meconium aspiration syndrome: historical aspects. *J Perinatol*. 2008; 28(3):S3-7.
- World Health Organization. Promoting optimal fetal development: report of a technical consultation. Geneva: World Health Organization; 2006.
- Lubchenco LO, Hansman C, Dressler M, Boyd E. Intrauterine growth as estimated from live born birth weight data at 24 to 42 weeks of gestation. *Pediatrics*. 1963; 32(5):793-800.
- Mukhtar-Yola M, Iliyasu Z. A review of neonatal morbidity and mortality in Aminu Kano teaching hospital, Northern Nigeria. *Trop Doct*. 2007; 37(3):130-2.
- Walana W, Acquah Ekuban KS, Abdul-Mumin A, Naafu B, Aruk E, Vicar KE. Pattern, causes and treatment outcomes of neonatal admission in the Tamale teaching hospital. *Clin Mother Child Health*. 2016; 13(252):2.
- Hussain S. Neonatal morbidity and mortality pattern in a tertiary care neonatal unit of a teaching hospital. *Ann Pak Inst Med Sci*. 2014; 10(1):7-11.
- Mekonnen T, Tenu T, Akilu T, Abera T. Assessment of neonatal death and causes among admitted neonates in neonatal intensive care unit of Mizan Tepi University Teaching Hospital, Bench Maji Zone, South-West Ethiopia, 2018. *Clin Mother Child Health*. 2018; 15(305):2.
- Tekleab AM, Amaru GM, Tefera YA. Reasons for admission and neonatal outcome in the neonatal care unit of a tertiary care hospital in Addis Ababa: a prospective study. *Res Rep Neonatol*. 2016; 6:17-23.
- Demisse AG, Alemu F, Gizaw MA, Tigabu Z. Patterns of admission and factors associated with neonatal mortality among neonates admitted to the neonatal intensive care unit of University of Gondar Hospital, Northwest Ethiopia. *Pediatr Health Med Ther*. 2017; 8:57.
- Tewabe T, Mehariw Y, Negatie E, Yibeltal B. Neonatal mortality in the case of Felege Hiwot referral hospital, Bahir Dar, Amhara Regional State, North West Ethiopia 2016: a one year retrospective chart review. *Ital J Pediatr*. 2018; 44(1):1-5.
- Kumar R, Mundhra JA, Jain S. Morbidity and mortality profile of neonates admitted in special newborn care unit of a teaching hospital in Uttarakhand, India. *Int J Res Med Sci*. 2019; 7(1):241-6.
- Hoque M, Haaq S, Islam R. Causes of neonatal admissions and deaths at a rural hospital in KwaZulu-Natal, South Africa. *South Afr J Epidemiol Infect*. 2011; 26(1):26-9.
- Pongou R. Why is infant mortality higher in boys than in girls? A new hypothesis based on preconception environment and evidence from a large sample of twins. *Demography*. 2013; 50(2): 421-44.
- Toma BO, Ige OO, Abok II, Onwuanaku C, Abah RO, Donli A. Pattern of neonatal admissions and outcome in a tertiary institution in north central Nigeria. *J Med Trop*. 2013; 15:121-5.
- Babaei H, Dehghan M. Study of causes of neonatal mortality and its related factors in the neonatal intensive care unit of Imam Reza hospital in Kermanshah, Iran during (2014-2016). *Int J Pediatr*. 2018; 6(5):7641-9.
- Steer P. The epidemiology of preterm labor a global perspective. *J Perinatal Med*. 2005; 33(4):273-6.
- Ali SR, Ahmed S, Lohana H. Disease patterns and outcomes of neonatal admissions at a secondary care hospital in Pakistan. *Sultan Qaboos Univ Med J*. 2013; 13(3):418-21.
- Ugwu GI. Pattern of morbidity and mortality in the newborn special care unit in a tertiary institution in the Niger Delta region of Nigeria: a two year prospective study. *Glob Adv Res J Med Med Sci*. 2012; 1(6):133-8.
- Kumor MK, Thakur SN, Singh BB. Study of morbidity and the mortality patterns in NICU at tertiary care teaching hospital in Rohtas district, Bihar, India. *JCDR*. 2012; 6(2):282-5.

28. Parkash J, Das N. Pattern of admissions to neonatal unit. *J Coll Phys Surg Pak*. 2005; 15(6):341-4.
29. Zulfiqar R. Neonatal mortality: review from a tertiary hospital in Rawalpindi. *J Rawalpindi Med Coll*. 2009; 13(1):2-6.
30. Islam MN. Situation of neonatal health in Bangladesh Orion 2006. Available at: ULR: <http://www.criogroup.net/orion/20> medical journal vol.6; 2015.