

High Magnitude of Neonatal Anemia Among Sick Newborns Admitted to University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia

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Introduction: Anemia is a global health problem that affects all ages, particularly children under five years. If not treated early, childhood anemia results in impaired growth, delayed cognitive development, and organ dysfunction. There is a scarcity of studies on the prevalence of anemia among hospitalized sick neonates, especially in developing countries.

Objective: This study aimed to determine the magnitude of anemia and associated factors among hospitalized sick newborns at the University of Gondar Comprehensive Specialized Hospital (UOGCSH).

Methods: An institutional-based cross-sectional study was conducted among admitted newborns from June 1 to September 30, 2020. All newborns whose gestational age (GA) ≥ 28 weeks and postnatal age ≤ 28 days, admitted to UOGCSH during the study period were included in the study. Data were collected by pediatric residents and a systematic random sampling technique was used to select the study participants. Statistical analysis was performed using SPSS version 20. Binary logistic regression was used to identify associated factors with neonatal anemia. P-value < 0.05 was considered statistically significant.

Results: During the study period, 272 newborns were enrolled. The mean hemoglobin value was 15.74 ± 4.27 gm/dL. The prevalence of neonatal anemia in the study population was 30.1% (95% CI: 24.6–35.7). Neonatal age > 7 days (AOR = 4.41, 95% CI: 1.86–10.5), maternal anemia (AOR = 9.93, 95% CI: 4.36–21.6), antepartum hemorrhage (AOR = 4.05, 95% CI: 1.54–10.7), being multiple births (AOR = 4.70, 95% CI: 1.73–12.8), subgaleal hemorrhage (AOR = 7.56, 95% CI: 1.87–30.6), and hyperbilirubinemia (AOR = 3.84, 95% CI: 1.58–9.31) were associated with neonatal anemia.

Conclusion and Recommendation: The prevalence of anemia among hospitalized newborns was high. The current study recommends that healthcare providers should screen anemia among sick newborns who had risk factors. Prevention of maternal anemia and early treatment of obstetric complications will reduce the burden of anemia in sick neonates.

Keywords: newborns, neonatal anemia, associated factors, Ethiopia

Introduction

Anemia is defined by a hemoglobin or hematocrit value that is more than two standard deviations below the mean for age.^{1,2} Anemia is a global health problem that affects all ages.^{3,4} Based on the World health organization (WHO) 2011 report, the global estimated prevalence of anemia was 47% among under-five children.^{3,5} The prevalence of anemia in newborns varies and its prevalence rate ranges from 10 to 60%; being the highest range led by African countries.^{6–9} In general, the mechanisms of anemia are blood loss, decreased RBC production, and increased destruction of RBCs.^{10,11} Anemia in the newborn period is unique to other age groups that in addition to the above mechanisms, hemorrhagic/hemolytic conditions, gestational age-dependent variation of hemoglobin, and transition period to extrauterine life contributed to neonatal anemia.^{12,13} In addition to these, heavy phlebotomy, fast-growing period of the infants, and impaired ability to increase erythropoietin (EPO) appropriately in a setting of anemia are causes of neonatal anemia, especially in preterm newborns.^{14,15}

Anemia in newborn infants and children can result in acute organ dysfunction like heart failure, respiratory distress, depressed sensorium, or multi-organ failure due to poor oxygen delivery to vital tissues.^{16–18} The long-lasting consequences of anemia could result in growth failure, impaired neurocognitive development, and increased susceptibility to infection in all stages of age due to chronic hypoxia.^{4,16,18} Because of the high prevalence and poor health outcomes of anemia in children, it is considered a contributing factor to infant and childhood mortality.^{9,19,20}

To reduce the high burden of anemia in newborns, it is wise to consider and address risk factors. The risk factors for neonatal anemia also vary depending on the settings.^{7–9,13,15,21} In previous studies, contributing factors for neonatal anemia included maternal anemia,^{7,8,22} maternal malaria attack during pregnancy,^{7,21} maternal antepartum hemorrhage (APH),^{7,23} lack of iron-folate supplements during pregnancy,²³ maternal vegetable consumption habit,⁹ septicemia in the newborn,^{7,16} prematurity¹³ and other neonatal problems including external blood loss.^{15,16}

Several studies have been conducted to measure the prevalence of anemia in newborns. However, almost all of these studies used cord blood for hemoglobin analysis at the time of delivery and did not involve hospitalized sick neonates. None of these studies included the whole period of neonatal age (1–28 days). Hence, prior studies do not represent the prevalence of anemia in sick newborns and the entire neonatal period. We believed that these two conditions and other neonatal factors could directly or indirectly affect neonatal hemoglobin levels. Therefore, the present study aimed to determine the prevalence of anemia and its associated factors among sick neonates regardless of their postnatal age and medical illness.

Methodology

Study Design, Area, and Period

An institution-based prospective cross-sectional study was conducted among sick newborns admitted to UOGCSH neonatal intensive care unit from June 1, 2020, to September 30, 2020. UOGCSH is one of the oldest academic and referral hospital in the country, which is located northwest of Ethiopia. The neonatal ward in the hospital is a level III NICU which provides the maximum care for all admitted neonates with gestational age (GA) ≥ 28 weeks. The care is provided by senior pediatricians, pediatric residents, general practitioners, and neonatal nurses. The average number of admissions is 200 patients per month. The common causes of admission are neonatal sepsis, prematurity, perinatal asphyxia, and neonatal jaundice.

Study Participants

All sick newborns admitted to the neonatal ward at UOGCSH.

Eligibility Criteria

Inclusion Criteria

All sick newborns whose GA ≥ 28 weeks and postnatal age ≤ 28 days, admitted to the neonatal ward during the study period were included in the study.

Exclusion Criteria

Those newborns whose mothers refused to participate in the study, stayed < 24 hours in the ward, admitted for a surgical procedure, and newborns who are abandoned were excluded.

Sampling Size and Sampling Techniques

The sample size was calculated by using single population proportion formula assuming the prevalence of anemia in newborns was 25%,⁹ 95% CI ($Z = 1.96$), and 5% marginal error ($w = 0.05$), adding 5% non-respondents making the final sample size of 302. A systematic random sampling technique was used to select the study participants based on their medical record numbers. The estimated number of admissions in the study period was about 800 based on the admission discharge registry. The interval k was 2.7. Every 3rd newborn was taken from the sampling frame. The first sample was the first medical record number on the first date of data collection.

Data Collection Tools and Procedure

After enrollment, data were collected with pre-tested structured questionnaires containing the following information: socio-demographic characteristics of the mother and the newborn, medical and obstetric condition of the mother, and clinical status of the newborn. Two trained pediatric residents were data collectors. The principal investigators actively supervised the data collection throughout the data collection period for data completeness. After interviewing the mother, the charts of both the mother and the newborn were reviewed for further information. The hemoglobin ordered by the treating physician at admission was used for the newborn and a recent maternal hemoglobin value was obtained from the record review.

Data Compilation and Analysis

The data were checked for completeness, then coded and entered to Epi-info version 7.2.1.0 and exported to SPSS version 20.0 for analysis. Data were reported as mean/median and SD for continuous variables and frequency and percentage for categorical variables. Bivariable and multivariable logistic regression methods were used to identify the associated factors. Multivariable logistic regression is used on the backward step if $p < 0.2$ on bivariable analysis. In multivariable logistic regression, a p -value < 0.05 was considered statistically significant. The results of these models were expressed as 95% confidence interval and odd ratios.

Operational Definition

Newborn: An infant whose age is ≤ 28 days and delivered after 28 weeks of gestational age.

Sick newborn: Newborn who was admitted to the neonatal intensive care unit (NICU) for medical treatment.

Preterm neonate: Newborn delivered before completed 37 weeks of gestational age.

Neonatal anemia: Hemoglobin < 13 gm/dL for GA ≥ 28 weeks in the first 28 days of life.

Moderate anemia: Hemoglobin value between 7 gm/dL-10 gm/dL.

Severe anemia: Hemoglobin < 7 gm/dL.

Maternal anemia: Hemoglobin < 11 gm/dL.

Ethical Considerations

The study protocol was reviewed and approved by the ethical review board of the School of Medicine, the University of Gondar in accordance with the declaration of Helsinki. The ethical review board provided an approval letter with the reference number ERB2101/2020. Written informed consent prepared in the local language (Amharic) was obtained from the parents of the study participants after the aim of the study was explained. All parents were informed of their right to withdraw from the study at any stage of the interview or to restrict their data from data analysis. All personal information of the study participants was kept confidential and their name was not mentioned in the study.

Results

Socio-Demographic Characteristics of the Study Participants

From the total of 302 randomly selected neonates, 272 newborns fulfilled the inclusion criteria and 30 were excluded (21 incomplete documentation and 9 of them did not give consent). The male to female ratio of the study participants was 1.4:1. The average GA of the newborns was 37.3 ± 2.9 weeks. One-third of the newborns were born to maternal age less than 20 years (Table 1).

Obstetric and Perinatal Profile of the Mother and Study Newborns

Most mothers had antenatal care (ANC) follow-up during pregnancy, 87% reported taking iron and folic acid for at least 1 month before delivery. More than three-fourth (79%) of the newborns were delivered by spontaneous vaginal delivery. About 87% of the newborns were singleton. Nearly one-fourth of the mothers had anemia during pregnancy while 10% of mothers had antepartum bleeding during the current gestation (Table 2).

Table 1 Socio-Demographic Characteristics of the Study Participants (N = 272) Admitted to UOGCSH, 2020

Variable	n (%)
Age at admission	
<72hr	201 (74)
3 days-7 days	24 (9)
7–28 days	47 (17)
Sex	
Male	161 (59)
Female	111 (41)
GA	
<37 weeks	82 (30)
37–42 weeks	186 (68)
>42 weeks	4 (2)
Birth weight (gram)	
1000–2499	90 (33)
2500–4000	173 (64)
>4000	9 (3)
Maternal age(years)	
< 20	93 (34)
25–35	99 (36)
>35	80 (30)
Education status	
Unable to read and write	34 (13)
Primary education	122 (45)
Secondary education	36 (13)
College and above	80 (29)
Occupation	
Employed	104 (38)
Daily laborer	9 (3)
Farmer	102 (38)
Housewife	57 (21)
Residence	
Urban	124 (46)
Rural	148 (54)

Clinical and Laboratory Parameters of the Study Participants

The commonest reason for admission to the NICU was sepsis (89%) followed by prematurity (30%) (Table 3).

The mean hemoglobin value was 15.74 ± 4.27 gm/dL. The overall prevalence of neonatal anemia was 30.1% (95% CI: 24.6–35.7), of which 1.8% had severe anemia (Figure 1). The prevalence of anemia among preterm and terms was 31.7% and 29.5%, respectively.

Factors Associated with Neonatal Anemia in the Study Participants

Multivariate logistic regression output showed that neonatal age, maternal anemia, APH, subgaleal hemorrhage, multiple births, and hyperbilirubinemia were statistically associated with neonatal anemia as shown in (Table 4).

Discussion

We found that the burden of neonatal anemia among hospitalized neonates was 30.1% and 1.8% of the hospitalized neonates had severe anemia. The WHO considers this to be a moderate public health problem which is defined as 20–39.9%.²⁴ The finding in this study is similar to the studies done in Gondar, Ethiopia, 25%,⁹ Nigeria, 28.9%,²⁰ Brazil, 32.5%,²⁵ and Bosnia, 29.3%¹³ but

Table 2 Obstetric and Perinatal Profiles of the Mother and Newborns (N = 272) Admitted at the UOGCSH, 2020

Variables	n (%)
Parity	
Primiparous	114 (42)
Multiparous	158 (58)
Fetal number	
Singleton	236 (87)
Multiple	36 (13)
Mode of delivery	
Vaginal	214 (79)
C/S	46 (17)
Instrumental assisted	12 (4)
Place of delivery	
Hospital	207 (76)
Health center	54 (20)
Home	11 (4)
ANC follow up	
Had ANC follow up	238 (87)
No ANC follow up	34 (13)
Iron & folic acid	
took \geq 1 month	238 (87)
Did not take	34 (13)
Bleeding History	
Had APH	29 (11)
No APH	243 (89)
Maternal anemia	
Yes	59 (22)
No	213 (78)
HIV/AIDS	
Yes	4 (2)
No	268 (98)
Malarial attack history	
Yes	12 (4)
No	260 (96)
Maternal Malnutrition	
Yes	4 (2)
No	268 (98)

Abbreviations: APH, antepartum hemorrhage; ANC, antenatal care.

higher than the studies done in Addis Ababa, Ethiopia, 9%,²² USA, 21%,⁸ India, 19.4%,²⁶ the Netherlands, 21%,²⁷ and Iran, 11.7%.²⁸ This variation in the prevalence might be due to the differences in socio-demographic characteristics of the study populations, sample size, presence/absence of risk factors, and timing of hemoglobin determination. Most of the above studies did not assess important risk factors for neonatal anemia like maternal and obstetric conditions (APH, multiple pregnancy, HIV/AIDS, and Malaria),^{9,22} and used the cord blood for hemoglobin value, unlike the current study. In all the studies done in Ethiopia, only term neonates were included^{9,22,23} whereas only preterms were included in Bosnia.¹³ None of the studies included the entire neonatal period, which could affect the prevalence of anemia in the newborn due to physiological reduction of hemoglobin in the postnatal life.

There was no statistically significant difference in the prevalence of anemia among preterm neonates (31.7%) from term neonates (29.5%), which is similar to the study done in India.¹⁶ This lack of difference in prevalence could be

Table 3 Clinical Characteristics of the Study Participants (n = 272) Admitted to UOGCSH, 2020

Variables	n (%)
Prematurity	82 (30)
Hyperbilirubinemia	54 (20)
Perinatal Asphyxia	51 (19)
Sepsis ± meningitis	241 (89)
Acute bleeding	6 (2)
ABO/RH hemolytic diseases	15 (6)
Subgaleal hemorrhage	20 (8)
RDS	29 (11)
Severe pneumonia	17 (6)

Abbreviation: RDS, respiratory distress syndrome.

because we defined anemia as hemoglobin value less than 13 gm/dL for both preterm and term neonates which might not be the reality, especially in the first 2–3 months of postnatal life.

On the other hand, the prevalence in our study was lower than the studies in Benin, 61.1%,²⁹ Ghana, 57.3%,³⁰ and Iran, 53%.²¹ The explanations for the difference in these studies could be because newborns in these studies were born to mothers who had medical and obstetric conditions. In the study in Benin, all newborns were born to mothers who had a malaria attack during pregnancy. In Ghana; all the newborns were born to HIV-infected mothers. Finally in Iran, all the newborns were born to RH sensitized mothers. In these studies, there may be the possibility of congenital transmission of malaria and HIV causing hemolysis and bone marrow suppression resulting in a higher rate of anemia among the study newborns. RH hemolytic diseases of the newborn is the leading cause of anemia and hyperbilirubinemia in a neonate born from sensitized mothers, which could explain the higher prevalence of anemia in Iranian study.

In the current study, newborns who were born to anemic mothers during pregnancy had ten times the odds of developing neonatal anemia (AOR = 9.93, 95% CI: 4.36–21.6) than newborns born to non-anemic mothers, which was supported by studies done at St. Paul Hospital, Addis Ababa, Ethiopia²² and a study done in India.⁷ This may be due to inadequate transfer of iron, folate, and vitamins to the fetus during pregnancy, which are essential substrates for hemoglobin synthesis in the fetus.³¹ Previous

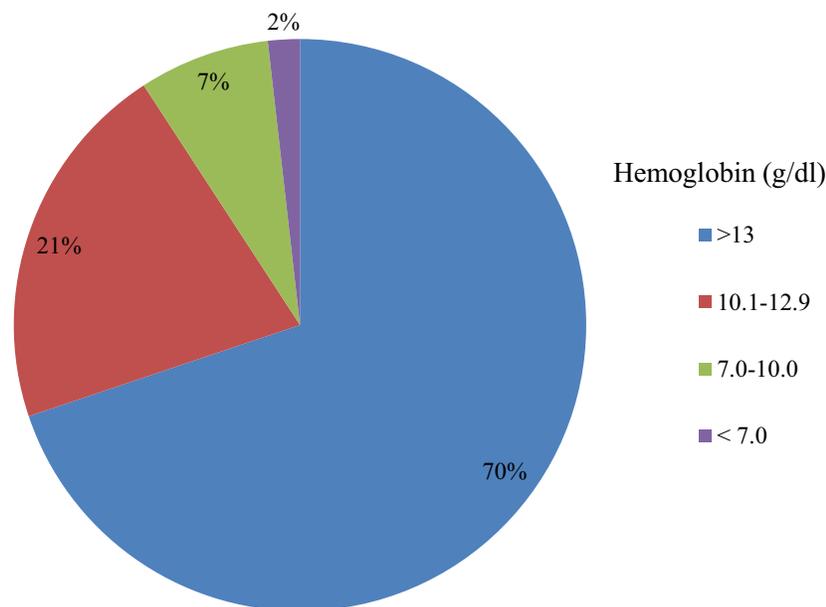


Figure 1 Hemoglobin profiles of the study participants (N = 272) admitted to UOGCSH, 2020.

Table 4 Bi-Variable and Multivariable Logistic Analysis of Factors Associated with Neonatal Anemia Among Newborns Admitted to UOGCSH, 2020 (N = 272)

Variables		Anemia	No Anemia	COR (95%, CI)	AOR (95%, CI)	P-value
Education status	Unable to read andwrite	10	24	1.44(0.58–3.56)	0.97(0.12–8.17)	0.982
	Grade 1–8	39	83	1.62(0.85–3.09)	1.19(0.17–8.44)	0.760
	Grade 8–12	15	21	1.62(0.85–3.10)	1.50(0.45–4.99)	0.439
	College & above	18	62			
Maternal Anemia	Yes	38	21	6.95(3.71–13.02)	9.93(4.36–21.64)	<0.001*
	NO	44	109			
Neonatal age	≤7 days	59	165			
	> 7 days	23	25	2.57(1.36–4.88)	4.41(1.86–10.47)	<0.001*
Mode of delivery	Vaginal	63	151	1.33(0.63–2.78)	1.54(0.57–4.12)	0.990
	Instrument	8	4	6.36(1.60–25.25)	5.53(0.69–43.11)	0.154
	C/S	11	35			
ANC	Yes	68	170	1.75(0.84–3.66)	0.97(0.34–2.80)	0.158
	No	14	20			
APH	Yes	16	13	3.30(1.51–7.23)	4.05(1.54–10.70)	0.006*
	No	66	177			
Fetus	Singleton	66	170			
	Multiple	16	20	2.06(1.10–4.22)	4.70(1.73–12.81)	0.002*
Subgaleal hemorrhage	Yes	12	8	3.90(1.53–9.95)	7.56(1.87–30.60)	0.007*
	No	70	182			
Hyperbilirubinemia	Yes	25	29	2.44(1.32–4.50)	3.84(1.58–9.31)	<0.001*
	No	57	161			

Notes: *p-value < 0.05.

Abbreviations: COR, crude odds ratio; AOR, adjusted odds ratio.

studies in Ethiopia investigated that, the common causes of maternal anemia in pregnant women were iron and folate deficiency, hookworm infection, malaria attack, and HIV infection.^{32–34} As per the WHO and Ethiopian obstetric national guidelines for ANC follow-up, iron and folate daily supplementation is recommended as early as the first trimester till delivery to prevent maternal anemia and low birth weight.^{35,36} Regarding the adherence of pregnant women to these protocols in the study area, a recent systematic review and meta-analysis study was done in Ethiopia which showed the overall prevalence of adherence to iron-folate supplementation was low (41%).³⁷

In addition, in this study, neonatal anemia was also strongly associated with antepartum hemorrhage (AOR = 4.05, 95% CI: 1.54–10.70) during pregnancy which was a similar finding in a study done in India^{7,38} and Scotland.³⁹ Bleeding during pregnancy and delivery might lead to a compromised placental transfer of nutrients and an ongoing fetomaternal hemorrhage in the newborn as well.

In the present study, anemia was strongly associated with multiple births, which was supported by a study done in the USA from 2011 to 2014.²⁷ Multiple pregnancies might increase twin-twin transfusion and antepartum bleeding during pregnancy, which could contribute to neonatal anemia among the study populations.

Anemia was also more often seen in newborns after the first week of life (AOR = 4.41, 95% CI: 1.86, 10.5), which is different from the study done in India.⁷ The higher magnitude of anemia after the first week of life in this study could be due to many reasons in the study population. These include either an exaggerated physiological reduction of hemoglobin in the first few months of postnatal life, repeated laboratory sampling, or bleeding from common cultural traditional malpractices (uvulectomy, circumcision) in the study population which are being done after the first week of life.

In the current study, anemia was significantly associated with hyperbilirubinemia which was a similar finding in a study done in India.⁷ Anemia and hyperbilirubinemia are related mainly by causative factors. The most common causes of hyperbilirubinemia in this study could be either due to Rh/ABO hemolytic diseases of the newborn, prematurity, subgaleal hemorrhage, or perinatal infection that directly or indirectly affect neonatal anemia.⁴⁰

Moreover, neonatal anemia in this study was also associated with subgaleal hemorrhage in the newborn (AOR = 7.56, 95% CI: 1.87–30.60). Anemia is the most common complication of subgaleal hemorrhage either due to acute bleeding in

the enclosed space (sub aponeurotic space or subperiosteal collection) or ongoing hemolysis, which could explain the high burden of anemia in our study population.⁴¹

The main strength of this study was that it is a prospective study; one of the very few studies in sick neonates admitted to the tertiary hospital across the world and assessed various contributing neonatal factors for anemia. However, it had to be interpreted with limitations. This is a cross-sectional study, which limits establishing a temporal relationship between variables that were studied. We did not identify the causes of anemia. We used the same hemoglobin cut-off value to define anemia in both term and preterm neonates to be consistent with other studies. In reality, the hemoglobin cut-off value in preterm is a bit lower than in term newborns, especially during the first 2–3 months of life.

Conclusions

The current study showed that the prevalence of neonatal anemia among hospitalized neonates was high. Maternal anemia, APH, multiple births, neonatal age, and subgaleal hemorrhage were strongly associated with neonatal anemia.

Recommendation

We recommend that healthcare providers should screen neonatal anemia among sick newborns who had risk factors. Future studies in different settings are beneficial to routinely recommend neonatal anemia screening on NICU guideline protocol. Prevention of maternal anemia and early treatment of obstetric complications will reduce the burden of anemia in newborns. Newborns with anemia should require further investigations to identify the cause and early intervention.

Abbreviations

ANC, antenatal care; AOR, adjusted odds ratio; APH, antepartum hemorrhage; COR, crude odd ratio; C/S, cesarean section; GA, gestational age; MRN, medical registration number; NICU, neonatal intensive unit; LBW, low birth weight; RDS, respiratory distress syndrome; UOGCSH, University of Gondar Comprehensive and Specialized Hospital.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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