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Epidemiology and Associated Factors with Anemia in Premature Newborns at the Issaka Gazoby Maternity Hospital of Niamey (Niger) in 2023

Samaila Aboubacar[1,2*], Garba Moumouni[1,2], Georges Thomas Ibrahim[3], Mamoudou Abdou Djafar[4], Gagara Mayaou Adama[5], Mededji Marlix[5], Moussa Nanaito Nafissatou[6], Djibrilla Almoustapha Amadou[2,6], Kamaye Moumouni[2,4], Malam Abdou Bade[2,6]

[1]Department of Paediatric, Amirou Boubacar Diallo National Hospital, Niamey, Niger
[2]Faculty of Health Sciences, Abdou Moumouni University, Niamey, Niger
[3]Faculty of Health Sciences, André Salifou University of Zinder, Zinder, Niger
[4]Department of Paediatric, National Hospital of Niamey, Niamey, Niger
[5]Issaka Gazoby Maternity Hospital of Niamey, Niamey, Niger
[6]Department of Onco-Haematology, National Hospital of Niamey, Niamey, Niger
Email: *samailaa1@gmail.com

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Abstract

Introduction: Anemia is common in premature newborns. The objective of this study was to examine the epidemiological aspects and associated factors with anemia in premature newborns at the Issaka Gazoby Maternity Hospital of Niamey in 2023. **Patients and Methods**: This was a case-control study conducted from January to June 2023 at the Issaka Gazoby Maternity Hospital in Niamey. The "cases" were newborns with anemia, and the "controls" were newborns with normal hemoglobin levels. The Odds Ratio and its Confidence Interval were calculated to measure the association. **Results**: Of the 617 premature newborns admitted during the study period, 158 cases of anemia were found (25.6%). Anemia was severe in 9.5% of newborns. The sex ratio was 1.6. The main clinical signs on admission were pallor (69.4%) and respiratory distress (59.3%). Associated factors related to perinatal characteristics were pregnancy monitoring with more than 4 prenatal consultations (OR = 0.56; CI [0.37 - 0.86]; p = 0.01), malaria prophylaxis (OR = 0.34; CI [0.20 - 0.60]; p < 0.01), and iron and folic acid supplementation (OR = 0.59; CI [0.36 - 0.97]; p = 0.04). The associated neonatal characteristics were birth before 33 weeks of gestational age (OR = 1.7; CI [1.16 - 2.51]; p < 0.01). **Conclusion**: Anemia is a major cause of hospitalization in premature newborn. Associated factors in-

cluded good prenatal care, iron and folic acid supplementation, and malaria prophylaxis, suggesting that these strategies should be reinforced.

Keywords

Anemia, Premature Newborn, Associated Factors, Niger

1. Introduction

Anemia is one of the most common conditions in the neonatal period, particularly in premature newborns. It is a pathological condition in which hemoglobin levels are insufficient to meet the body's physiological needs [1] [2]. According to the WHO report, premature births accounted for 13.4 million live births, with nearly 900,000 deaths [3] [4]. Deaths related to prematurity are attributable to common complications such as anemia. Little research has been devoted to studying anemia associated with prematurity in our context. The objective of this study was to examine the epidemiological aspects and factors associated with anemia in premature newborns in the Neonatology Department of the Issaka Gazoby Maternity Hospital of Niamey in 2023.

2. Patients and Methods

2.1. Type and Period of Study and Study Setting

This was a case-control study conducted over a six-month period from January to June 2023. It was carried out in the neonatal unit of the Issaka Gazoby Maternity Hospital in Niamey, one of the country's level 3 referral centers for neonatal health.

2.2. Study Population

Premature newborns hospitalized in the department constituted the study population. The "cases" were newborns who presented anemia. The "controls" were selected from newborns who had normal hemoglobin levels. For each "case," two (02) "controls" admitted on the same day were matched.

2.2.1. Inclusion Criteria

For "cases" and "controls," newborns with a medical record containing at least one blood count were included.

2.2.2. Non-Inclusion Criteria

Newborns whose mothers did not give their consent to participate in the study, both for "cases" and "controls," were not included.

2.2.3. Sampling Technique and Sample Size

The prevalence of anemia among premature newborn was 25% [5]. In the absence of data from the literature on "controls," a prevalence of 50% was used instead.

The following formula was used to calculate the sample size (WHO, 1991):

$$n = \left\{ z_{1-\alpha} \sqrt{2\bar{P}\left(1-\bar{P}\right)} + z_{1-\beta} \sqrt{P_1\left(1-P_1\right) + P_2\left(1-P_2\right)} \right\}^2 \Big/ \left(P_1 - P_2\right)^2$$

$$\bar{P} = \left(P_1 + P_2\right)/2$$

The minimum sample size required was 63 cases for a significant level of 5% and a power of 90%. Simple random convenience sampling was used.

2.3. Variables Studied

The main dependent variable was the presence of anemia in the newborn. The explanatory variables or groups of variables related to sociodemographic characteristics (gender, age, mother's age, presence of revenue-generating activity, level of education) and perinatal history (number of prenatal consultations [PNC], type and term of pregnancy, Antimalarial chemoprophylaxis based on sulfadoxine-pyrimethamine, iron and folic acid supplementation, place and mode of delivery). Links were also sought between neonatal characteristics (age, sex, birth weight), deaths and anemia.

2.4. Definition of Variables

Premature newborn was defined as birth with a gestational age of less than 37 weeks of amenorrhea (SA). Neonatal anemia was defined as a hemoglobin (Hb) level less than or equal to minus (-) 2 standard deviations (SD) from the mean hemoglobin level for gestational age and postnatal age. It was classified as mild when the Hb level was between 10 and 13 g/dL, moderate when the Hb level was between 8 and 10 g/dL, and severe when the Hb level was below 8 g/dL [6]. The blood sample for the complete blood count was taken upon admission of the newborns, prior to any treatment. Hypotrophy was defined as a weight < 10th percentile relative to the weight on gestational age curves [7]. Birth asphyxia was defined as an APGAR score < 7 at 5 minutes. Hypoglycemia was defined as a blood glucose level < 0.25 g/L (1.4 mmol/L) during the first three days of life and <0.30 g/L (1.6 mmol/L) thereafter.

2.5. Data Collection and Analysis

Data were collected from patient medical records and departmental registries. Analysis was performed using R Studio 4.1.1. In univariate analysis, Pearson's Chi-square test or Fischer's exact test were used with a significant threshold of 5% (p-value < 0.05). The crude odds ratio (OR) and its confidence interval (CI) were calculated. Variables with a p-value < 0.05 were then selected for multivariate regression. In multivariate etiological analysis, multiple logistic regression was performed to test the link between the explanatory variables and the central variable (anemia). For the adjustment strategy, a step-down approach was used. The results were expressed as adjusted OR (aOR) with their 95% CI. Variables for which the aOR were different from 1 and statistically significant were considered factors associated with anemia in premature newborns.

2.6. Ethical Aspects

The study was conducted after approval was obtained from the Issaka maternity hospital authorities and the head of the neonatal department. The data collected will remain anonymous, and confidentiality and medical secrecy have been respected.

3. Results

3.1. Characteristics of the Study Population

A total of 617 premature newborns were admitted to the department during the study period, including 158 cases of anemia, representing a frequency of 25.6% (Table 1). The mean hemoglobin level was 13.8 g/dL ± 2.9 [5.2 - 20.8 g/dL]. Anemia was severe in 9.5% of newborns. The sex ratio was 1.6. Newborns were less than 24 hours old in 94.3% of cases. The main clinical signs on admission were pallor (69.4%), respiratory distress (59.3%), and hypotonia (17.3%). In terms of laboratory findings, hypoglycemia and positive thick smear were found in 49.8% and 30.2% of patients, respectively. The main diagnoses, often associated in the same newborn, were neonatal infection (55%), perinatal asphyxia (42.3%), and congenital malaria (16.2%). Blood transfusions were performed in 13.3% of cases, and iron and multivitamin (A, D, E, C) supplementation was given to all newborns. Mortality rate was 31.6%. The main presumed causes of death were neonatal infection (50%), hyaline membrane disease (12.3%), and cyanotic congenital heart disease (5.2%).

Table 1. Hemoglobin status.

Hemoglobin level (N = 617)	Number (N)	Percent (%)
Normal	459	74.4
Anemia	158	25.6
Type of anemia (N = 158)		
Mild (>10 g/dL)	100	63.3
Moderate (8 - 10 g/dL)	43	27.2
Severe (<8 g/dL)	15	9.5

3.2. Maternal, Perinatal Characteristics, and Occurrence of Anemia

There was no statistically significant association between maternal age, income-generating activity, or educational level and the occurrence of anemia ($p > 0.05$). The relationship between perinatal characteristics and the occurrence of anemia is shown in Table 2. About pregnancy monitoring, having had four (4) or more antenatal care visits significantly protected against the occurrence of anemia (OR = 0.56; CI [0.37 - 0.86]; $p = 0.01$). Antimalarial chemoprophylaxis based on sulfadoxine-pyrimethamine was also a statistically significant protective factor against

the risk of anemia (OR = 0.34; CI [0.20 - 0.60]; p < 0.01). The same was true for iron and folic acid supplementation (OR = 0.59; CI [0.36 - 0.97]; p = 0.04). Most anemia cases occurred in monofetal pregnancies (89.2%), with no link to the occurrence of anemia (p > 0.05). There was also no statistically significant link between the place and mode of delivery and the occurrence of anemia in premature newborns (p > 0.05).

Table 2. Perinatal characteristics and the occurrence of anemia.

Variable	Status		OR [CI]	p
	Case N (%)	Controls N (%)		
Number of prenatal consultations				
≥4	54 (34.2)	72 (22.8)		
<4	104 (65.8)	244 (77.2)	0.56 [0.37 - 0.86]	0.01
Antimalarial chemoprophylaxis				
Yes	18 (11.4)	85 (26.9)		
No	140 (88.6)	231 (73.1)	0.34 [0.20 - 0.60]	<0.01
Iron and folic acid supplementation				
Yes	27 (17.1)	81 (25.6)		
No	131 (82.9)	235 (74.4)	0.59 [0.36 - 0.97]	0.04
Type of pregnancy				
Monofetal	141 (89.2)	263 (83.2)		
Multiple	17 (10.8)	53 (16.8)	1.67 [0.93 - 2.99]	0.10
Place of delivery				
Health center	152 (96.2)	310 (98.1)		
Home	6 (3.8)	6 (1.9)	0.49 [0.15 - 1.54]	0.35
Mode of delivery				
Cesarean section	77 (48.7)	175 (55.4)		
Vaginal delivery	81 (51.3)	141 (44.6)	1.3 [0.89 - 1.91]	0.20

3.3. Neonatal Characteristics and Occurrence of Anemia

Table 3 shows neonatal characteristics and the occurrence of anemia. Newborns born before 33 weeks of gestational age have a 1.7 times higher risk of anemia (OR = 1.7; CI [1.16; 2.51]; p < 0.01). There was no statistically significant association between the sex of the newborn, age at admission, presence of hypotrophy, and occurrence of anemia (p > 0.05). Deaths were observed in 31.6% of cases compared with 26.9% of controls, with no statistically significant link (p > 0.05).

Table 3. Neonatal characteristics and the occurrence of anemia.

Variable	Status		OR [CI]	p
	Case N(%)	Controls N(%)		
Term at birth (weeks of amenorrhea)				
<33 WA	86 (54.4)	130 (41.1)		
≥33 WA	72 (45.6)	186 (58.9)	1.7 [1.16 - 2.51]	<0.01
Sex				
Femal	61 (38.6)	124 (39.2)		
Male	97 (61.4)	192 (60.8)	0.97 [0.65 - 1.44]	0.97
Age at admission (Hours)				
<24 H	149 (94.3)	307 (97.2)		
≥24 H	9 (5.7)	9 (2.8)	2.06 [0.80 - 5.29]	0.20
Hypotrophy				
Yes	54 (34.2)	89 (28.2)		
No	104 (65.8)	227 (71.8)	0.75 [0.50 - 1.13]	0.21
Discharge status				
Dead	50 (31.6)	85 (26.9)		
Recovered	108 (68.4)	231 (73.1)	1.25 [0.82 - 1.90]	0.28

3.4. Multivariate Analysis of Associated Factors

On multivariate analysis (Table 4), factors associated with anemia in premature newborns were antimalarial chemoprophylaxis (aOR = 0.34 [0.20 - 0.60]; p < 0.01]) and Iron and folic acid supplementation (aOR = 0.19 [0.05 - 0.66]; p < 0.01).

Table 4. Multivariate analysis.

Variable	Anemia [N (%)]	aOR [CI]	p
Prenatal consultations ≥ 4	54 (34.2)	1.55 [0.67 - 3.62]	0.30
Antimalarial chemoprophylaxis	18 (11.4)	0.34 [0.20 - 0.60]	<0.01
Iron/ folic acid supplementation	27 (17.1)	0.19 [0.05 - 0.66]	<0.01
Gestational age < 33 WA	86 (54.4)	1.67 [0.93 - 2.99]	0.10

4. Discussion

This study, the first of its kind at the Issaka Gazoby maternity hospital in Niamey, highlighted several factors associated with the occurrence of anemia in premature newborns. The limitations or potential biases were also related to the retrospective nature of the study, which reduced the number of variables that could be explored. Furthermore, certain factors traditionally associated with the onset of anemia in premature newborns were not explored in this study. These include the iron status

of the mother and newborn, and the measurement of other vitamins and hormones (erythropoietin), which are not feasible in our context.

Anemia in premature newborns is a common condition in the neonatal unit at the Issaka Gazoby Maternity Hospital due to its frequency. Other authors have reported varying frequencies, ranging from 10% to 30% [5] [8]-[10]. The differences in rates often depend on the methodologies used, particularly regarding the definition of anemia cases. This high frequency of anemia in premature newborns reflects its multifactorial origin. On the one hand, the immaturity of their hematopoietic organs exposes them to anemia more than full-term newborns. In addition, there is a transient deficiency of erythropoietin, the main hormone involved in hematopoiesis [1]. Apart from these etiological factors, there are hemorrhagic complications that can cause anemia. These include hemorrhagic disease of the newborn, as well as cerebral hemorrhages, particularly intraventricular hemorrhages [4]. Some authors have reported repeated blood sampling for laboratory tests as a risk factor associated with the onset of anemia in newborns [11]. All these factors have led learned societies to recommend preventive measures for anemia in premature newborns. These include systematic iron and multivitamin supplementation and treatment with erythropoietin [7] [12] [13]. To limit blood loss, it has been recommended to delay cord clamping after delivery and to limit blood sampling [14].

About the characteristics of the mothers, most mothers of newborns with anemia were uneducated. Although this study found no link between maternal education and the occurrence of anemia, it has been shown that educated mothers are more receptive to advice on care and therefore on the prevention of certain risk situations [15]. This study found that 4 or more pregnancy monitoring was associated with a reduced risk of anemia in premature newborns. In general, it is during pregnancy monitoring at PNC that many situations of maternal and neonatal morbidity are detected and managed. These are usually maternal conditions such as nutritional deficiencies, obstetric hemorrhages, and pregnancy-induced toxemia. PNC also provide an opportunity to investigate maternal anemia, which is one of the main causes of anemia and low birth weight. For all these reasons, the WHO now recommends at least one antenatal care visit per month during pregnancy [16].

Antimalarial chemoprophylaxis based on sulfadoxine-pyrimethamine in mothers provides statistically significant protection against anemia in premature newborns. Intermittent preventive treatment is a key intervention during pregnancy to reduce the risk of malaria in pregnant women, and therefore anemia. This treatment is recommended from the onset of active fetal movements until the end of pregnancy in all malaria-endemic countries [17]. Another systematic treatment in our context is iron supplementation. This therapeutic measure compensates for the physiological anemia of pregnant women. During pregnancy, anemia is mainly secondary to increased iron and folic acid requirements, which has led the WHO to recommend this treatment. In addition to its role in hematopoiesis, folic

acid is involved in the maturation of the fetal central nervous system [18]. Furthermore, in this study, iron and folic acid supplementation was a statistically significant protective factor against anemia. The type of pregnancy was not associated with the occurrence of anemia in premature newborns in this study. The same results have been reported by other authors in the subregion [8] [11] [19].

Males were more represented, as found by Lasme *et al.* and Eyebe *et al.*, without any statistically significant link [8] [20]. In contrast, Mah *et al.* reported a predominance of females, but no link with the occurrence of anemia. In addition, the latter study found a statistically significant risk of death among female newborns ($p = 0.002$) [19]. The proportion of very low birth weight (less than 1500 g) found in this study was lower than that reported by Dick-Amon F *et al.* (45%) [5]. Anemia has been reported as a risk factor for low birth weight [12]. In this study, clinical signs were dominated by pallor, respiratory distress, and hypotonia. Lasme Guillao *et al.* reported pallor (42.7%) as the most common clinical sign, followed by tachypnea (22.5%) and tachycardia (17.7%) [8]. Compared to associated pathologies in newborns, neonatal infection was the most common. Other authors have also found a significant association between infection and anemia, with frequencies ranging from 56.4% to 77% [8] [11] [21]. Anemia is a common complication of infectious diseases in general due to the acute hemolysis they cause. These infections affect 10% to 30% of premature newborns and are responsible for increased short- and long-term mortality and morbidity [12]. In this study, no statistically significant link was found between deaths in newborns and the presence of anemia, a result corroborated by the study by Koum *et al.* [21]. Anemia has been described as a major cause of neonatal morbidity and mortality by several authors, suggesting its systematic screening and adequate management [11] [19] [22].

5. Conclusion

Anemia in premature infants is a major cause of neonatal morbidity at the Issaka Gazoby Maternity Hospital. The factors associated with the onset of anemia were related to perinatal characteristics, including pregnancy monitoring, iron and folic acid supplementation, and antimalarial chemoprophylaxis based on sulfadoxine-pyrimethamine, suggesting that these strategies should be reinforced. Full-term delivery and hypotrophy also appear to be linked to the occurrence of anemia in premature newborns, hence the need to gain a few weeks before delivery. The aim is to prevent premature delivery and effectively manage associated pathologies in newborns to improve the prognosis.

Conflicts of Interest

There are no conflicts of interest.

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