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Determinants of anemia in premature newborns and the immediate outcome at the Mother and Child Center of the Chantal BIYA Foundation, Cameroon

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Abstract

Background: Anemia is a common and serious health problem, especially in premature infants. The objective of this study was to identify the determinants of anemia in premature infants and the factors influencing their hospital outcome. **Methods:** This was a retrospective study in the neonatal unit of the Mother Child Center of the Chantal Biya Foundation. Were included, all premature babies admitted between January 1, 2013 and December 31, 2017, who at least had a full blood count done. Data collected from medical records focused on maternal and neonatal characteristics, clinical and laboratory features, treatment received and hospital outcome. **Results:** Among the 425 premature babies included, 140 (32.9%) had anemia and 14 (10%) died. The risk factors for anemia in the premature infants were age at admission over 24 hours (p = 0.002) and gestational age less than 32 weeks (p <0.001). The factors associated with mortality were female sex (p = 0.030), birth weight <1500g (p = 0.029), gestational age <32 weeks (p = 0.024). The presence of respiratory distress (p = 0.009), thrombocytopenia (p = 0.011), the need for oxygen (p <0.001) and the need for blood transfusion (p = 0.004) were risk factors for death. However only bradycardia was an independent clinical feature associated with death (p = 0.037). **Conclusion:** Anemia is very common in premature babies, and remains a high risk factor for death. The clinical and laboratory monitoring of anemic premature babies must be rigorous especially in babies born very preterm and with very low birth weight.

Keywords: Anemia, Premature baby, Cameroon.

INTRODUCTION

In 2017, the neonatal mortality rate was 18‰ worldwide and 22 ‰ in Cameroon [1]. Complications of prematurity are the leading cause of neonatal mortality in Cameroon and one of these complications is anemia, defined as a hemoglobin level of less than two standard deviations (-2DS) from the mean hemoglobin value for postnatal age [2]. In premature babies, it corresponds to a hemoglobin level of less than 13 g / dl [3, 4]. Anemia is a common and fatal disease in premature infants if it is not properly and carefully managed [5]. The speed with which this anemia develops and its ultimate severity are determined by a combination of physiological and pathological processes including: hemorrhage, infections, insufficient nutrient intake and cardiorespiratory disease and iatrogenic causes [3-5]. An study carried out in Yaounde found a very high prevalence rate of anemia in premature babies (24.2%) [6]. In developed countries, red blood cell transfusion is the key treatment for anemia of prematurity together with use of iron and erythropoietin [3, 7, 8]. In low-income countries, the immediate management of anemia and hospital monitoring of premature babies remains difficult because of very limited resources [9]. However, it should be noted that although anemia of prematurity can not be absolutely prevented, its severity can be prevented. In order to improve the care of premature newborns and to contribute to the reduction and eventually elimination of avoidable newborn deaths. We studied the determinants of anemia in premature newborns and their immediate outcome at the Mother and Child Centre (MCC) of the Chantal Biya Foundation (CBF), which is one of the reference centers for the care of neonates in Cameroon.

MATERIALS AND METHODS

This was a cross-sectional retrospective study conducted at the Mother and Child Center of the Chantal Biya Foundation, which receives a large number of new-borns from the city of Yaoundé and its environs.

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Were included, all premature babies admitted to the neonatal unit of this centre between January 1, 2013 and December 31, 2017 and who had at least one full blood count done. We excluded all premature babies discharged against medical advice. The data was collected from medical records and for each premature infant meeting the inclusion criteria. We collected, data relating to neonates (Sex, gestational age, birth weight and age on admission), clinical and biological features, the treatment received and the hospital outcome and maternal data (socio-professional: Age, profession, and obstetrical data: antenatal clinic (ANC) pathologies during pregnancy, prophylaxis).

Anemia was considered in all premature babies with a hemoglobin level strictly below 13 g / dl. Hospital outcome was defined as survival or death after hospitalization. A file was considered incomplete when important information like birth weight, gestational age, or obstetrical data were missing.

The sample seize was calculated using the cochran formular (8). Data analysis was done using IBM SPSS version 20 software. Chi-square test and odds ratio (OR) with it's 95% confidence interval were used to find associations between the qualitative variables. Any difference was considered statistically significant for a p-value strictly less than 0.05. The Institutional Ethics and Research Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I approved the study.

RESULTS

We counted 653 premature babies admitted to the CME-FCB during the study period. Then, 33 babies were released against medical advice and 195 excluded because of incomplete records. The final study population consisted of 425 premature babies. Amongst which, 140 had a hemoglobin level <13 g / dl, for a hospital prevalence of anemia on prematurity of 32.9%. Male newborns numbered 58 (41.4%), for a sex ratio of 0.70. One hundred and nine (77.9%) premature babies were admitted within the first 24 hours of life. The birth weight varied between 850 and 2450g, with an average of 1678.2 ± 418.5g. The mean gestational age was 32.6 ± 2.3 weeks of amenorrhea ranging from 26 to 36 weeks (Table 1). There were no maternal characteristics associated with the occurrence of anemia in premature infants (Table 1). Regarding neonatal factors, age at admission less than 24 hours was a protective factor against anemia (aOR = 0.56, 95%CI (0.39-0.50), P= 0.002); while gestational age less than 32 weeks was a risk factor for anemia in premature infants (aOR 2.38 =95%CI(1.53-3.69), P <0.001. (Table 2).

Table 1: Maternal and neonatal characteristics associated with anemia in the study population

Factor = Variables	**Anemia**		**OR (95% CI)**	**p-Value**
	Yes N=140 (%)	**No N=285 (%)**		
Neonatal characteristics of premature babies				
Sex				
Female	82(58.6)	159(55.8)	1.12 (0.74-1.68)	0.586
Male	58(41.4)	126(44.2)		
Admission age (days)				
≤1	109(77.9)	244(85.6)	0.59 (0.35-0.99)	**0.045**
2-28	31(22.1)	41(14.4)		
Birth weight (gr)				
<1500	44(31.4)	67(23.5)	1.49 (0.95-2.33)	0.081
[1500-2500]	96(68,6)	218(76,5)		
Gestational age (weeks)				
<32	43(30.7)	42(14.7)	2.56 (1.58-4.17)	**<0.001**
[32-37]	97(69.3)	243(85.3)		
Vitamin K at birth (Yes)	70(50.0)	151(53.0)	0.89 (0.59-1.33)	0.563
Socio-demographic and obstetrical characteristics of mothers				
Age of mothers (years)				
< 20 and ≥35	24(17.1)	47(16.5)	1.04 (0.61-1.79)	0.866
[20-34]	116(82.9)	238(83.5)		
Professional class				
Unemployed	95(67.9)	206(72.3)	0.81 (0.52-1.25)	0.346
Employed	45(32.1)	79(27.7)		
Parity				
Primipare	81(57.9)	151(53.0)	1.21 (0.81-1.83)	0.343
Number of ANCs (≤ 3)	91(65.0)	162(56.8)	1.41 (0.92-2.14)	0.107
Anemia prophylaxis(Yes)	99(70.7)	195(68.4)	0.89 (0.57-1.39)	0.630
Malaria prophylaxis (Yes)	97(69.3)	216(75.8)	1.38 (0.88-2.17)	0.153
Pathologies in pregnancy				
Malaria	34(24.3)	71(24.9)	0.96 (0.60-1.54)	0.888
Urogenital infections	11(7.9)	22(7.7)	1.01 (0.48-2.16)	0.960

High blood pressure	4(2.9)	16(5.6)	0.49 (0.16-1.50)	0.207
HIV infection	18(12.9)	23(8.1)	1.68 (0.87-3.23)	0.116
Number of fetuses				
Mono-fetal pregnancy	84(60.0)	178(62.5)	0.90 (0.59-1.36)	0.625
Multiple pregnancy	56(40.0)	107(37.5)		
Mode of delivery				
Vagina	113(80.7)	233(81.8)	0.93 (0.55-1.56)	
Caesarean section	27(19.3)	52(18.2)		

Table 2: Independent factors associated with anemia in preterm

Variables	**OR(95%CI)**	**p-value**	**aOR (95%CI)**	**p-value**
Age on admission < 1 day	0.59 (0.35-0.99)	0.045	0.56 (0.39-0.80)	0.002
Gestational age <32 SA	2.56 (1.58-4.17)	<0.001	2.38 (1.53-3.69)	<0.001
Birth weight <1500g	1.49 (0.95-2.33)	0.081	0.96 (0.54-1.72)	0.904

Out of 140 anemic premature babies, 14 (10%) died. Factors associated with death were sex, birth weight less than 1500g, gestational age of less than 32 weeks.

Clinical signs associated to death included: convulsion, apnea, pallor, bradycardia, tachycardia, and tachypnea and the most frequently found pathology was respiratory distress. The only biological marker associated with mortality was thrombocytopenia, (Table 3).

Table 3: Factors associated with death in anemic preterm babies

Variables	**Anemia**		**OR (95%)**	**p-Val*ue***
	Deceased N=14 n (%)	**Survivors N=126 n (%)**		
Sex				
Female	12(85.7)	70(55.6)	4.80 (1.03-22.33)	**0.030**
Birth weight (gram)				
<1500	8(57.1)	36(28.6)	3.33 (1.08-10.28)	**0.029**
Gestational Age (weeks)				
<32	8(57.1)	35(27.8)	3.46 (1.12-10.71)	**0.024**
Clinical signs				
Pallor	10(71.4)	44(34.9)	4.65 (1.38-15.71)	0.008
Tachycardia	8(57.1)	38(30.2)	3.08 (1.00-9.50)	0.041
Tachypnea	9(64.3)	45(35.7)	3.24 (1.02-10.25)	0.037
Apnea	4(28.6)	9(7.1)	5.20 (1.35-19.92)	0.009
Convulsions	2(14.3)	2(1.6)	10.33 (1.33-80.07)	0.007
Bradycardia	4(28.6)	10(7.9)	4.64 (1.23-17.49)	0.015
Pathologies				
Respiratory distress	11(78.6)	53(42.1)	5.05 (1.34-18.99)	0.009
Platelet count (/mm3)				
<150000	7(50.0)	25(19.8)	4.04 (1.29-12.57)	0.011
≥150000	7(50.0)	101(80.2)		
Treatment				
Transfusion	11(78.6)	48(38.1)	5.95 (1.58-22.44)	0.004
Oxygen	10(71.4)	31(24.6)	7.66 (2.24-26.16)	<0.001

After logistic regression, only bradycardia was independently associated with death (**aOR=14.05, CI95=1.17-168.13**, **P= 0.03)** (Table 4).

Table 4: Independent factors associated with death in anemic preterm babies

Variables	**OR (95%CI)**	***p*-value**	**aOR (95%CI)**	***p*-Value**
Sex feminine	4.80 (1.03-22.33)	0.030	0.17 (0.01-1.95)	0.158
Very low birth weight	3.33 (1.08-10.28)	0.029	1.98 (0.26-14.85)	0.506
Gestational age	3.46 (1.12-10.71)	0.024	1.07 (0.11-9.78)	0.951
Pallor	4.65 (1.38-15.71)	0.008	2.63 (0.32-21.57)	0.366
Tachypnea	3.08 (1.00-9.50)	0.041	2.74 (0.44-17.02)	0.279
Tachycardia	3.24 (1.02-10.25)	0.037	1.85 (0.36-9.41)	0.454
Apnea	5.20 (1.35-19.92)	0.009	0.60 (0.06-5.28)	0.646
Bradycardia	10.33 (1.33-80.07)	0.007	14.05 (1.17-168.13)	0.037
Convulsions	4.64 (1.23-17.49)	0.015	8.69 (0.45-167.65)	0.152
Respiratory Distress	5.05 (1.34-18.99)	0.009	3.39 (0.67-17.09)	0.139
Thrombopenia	4.04 (1.29-12.57)	0.011	0.53 (0.10-2.66)	0.446
Oxygen	7.66 (2.24-26.16)	0.004	1.50 (0.14-15.53)	0.733
Blood transfusion	5.95 (1.58-22.44)	<0.001	0.93 (0.11-7.32)	0.949

DISCUSSION

The aim of our study was to identify the determinants of anemia in premature infants and the factors influencing the hospital outcome of premature infants with anemia. There were some weakness that can add bias to the results, given the retrospective nature of our study. The weakness is mainly due to missing clinical and laboratory data.

The prevalence of anemia in preterm infants in our study was 32.9%. This represents the prevalence in hospitalized neonates and may not reflect the real prevalence of neonatal anemia. This rate was similar to the rates reported by other African authors; 30% observed in Togo in 1992 [10], in Mali in 1994 more than one in 3 newborns presented with anemia and 24.2% found in Cameroon [6, 11]. On the other hand, it is higher than that reported by Folquet *et al* and Dick-Amon-Tanoh *et al* who found 17.5% and 25% respectively in Ivory Coast [11, 12]. This difference could be explained by the fact that the Ivorian studies only concerned anemia occurring during the first week of life. The prevalence of neonatal anemia found by Kedy *et al* in Cameroon was 57.2% [13]; however, her team assessed both term newborns and premature babies. These figures, although different, remain high regardless of the site and population involved, and should sound the alarm on the gravity of this often-neglected neonatal pathology. Moreover, it is well established that the newborn is particularly susceptible to anemia. This sensitivity is accentuated by the multiple neonatal pathologies directly affecting (hemolysis, infections, etc.) or indirectly (spoliation, hemorrhage, etc.) the red blood cell line [3, 7, 8].

The risk of developing anemia was higher in premature infants admitted after the 24th hour of life. Preterm babies have immature systems, and need immediate conditioning and treatment to prevent complications especially metabolic and infectious complications that can result in the need for investigations and even red cell destruction respectively worsening the physiologic decrease in hemoglobin level from birth [3, 4]. Hence, the protective nature of immediate admission and management of preterm against anemia.

It was found that, premature babies born before 32 weeks were twice as likely to be anemic during hospitalization; reflecting the findings of Hasanbegovic *et al* in Sarajevo in Bosnia in 2016 and This result is similar to that previously found by Abdelali in Morocco [14, 15]. However, he found that a good number of the patients born before 32weeks suffered from intracranial hemorrhage. It was not possible for us to check for this complication in our patients; however based on physical examination we did not find signs suggesting intracranial hemorrhage. On the other hand, infections and other metabolic complications like hypoglycemia and jaundice are very common in this category of patients and could be partly responsible for the anemia.

The death rate in preterm babies with anemia was 10%. This figure is lower than the 25.8% found in ivory cost and 21% reported in Sarjevo [12, 14]. This difference could be associated with commodities and treatment protocols as revealed by 60% co-infection reported by the Ivorian team.

Preterm with a birth weight of less than 1500g and a gestational age of less than 32 weeks were 3 times more likely to die. This result is similar to that previously described by Lopriore *et al* as well as Hasanbegovic *et al* and, the risk of death was about 5 times higher in girls [5, 14]. This was not the case in one study where the male sex was identified as a factor of mortality in premature anemic babies [15]. The reason for this difference was not clearly identified in our study. The only biological feature associated with mortality was thrombocytopenia, which increased the risk of death four-fold in premature anemic babies. Abdelali reported similar results [15]. The most frequent symptom in our study population was respiratory distress. Premature infants who had anemia associated with respiratory distress were five times more likely to die during hospitalization. The predominance of this pathology in our study could be explained by pulmonary immaturity probably due to the suboptimal use of antenatal corticosteroids on the one hand, and by hypoxia caused by the anemia itself on the other hand. The risk of death was approximately eight times higher in premature babies with anemia in whom oxygen therapy was indicated. This association between the need for oxygen and death could be explained by the fact that the main indication for oxygen therapy is respiratory distress, which was significantly associated with mortality. However, bradycardia was the only sign independently associated with death increasing the odds of dying by 14. Bradycardia is a last sign of cardiac failure, signally eminent cardiac arrest if nothing is done. This could mean that preterm infants should be monitored closely and action taken on time before exhaustion of the patient, other late action may not give desired result. This is further illustrated by the fact that amongst the premature babies who died, 78.6% received a transfusion. The deaths could been due to late initiation of transfusion resulting from difficulties in obtaining the blood on one hand and on the other hand lack of electronic monitoring equipment, so that monitoring is mainly manual, made worse by shortage of trained staff in our neonatal units.

CONCLUSION

The hospital prevalence of anemia in premature infants remains high, with a relatively high mortality rate. The clinical and biological monitoring of premature anemic babies must be rigorous especially in babies born very preterm and with very low birth weight, for quick action and prevention of death.

Conflicts of interest

The authors declare no conflict of interest.

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None declared.

Author contributions

EM, POKN designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. KTDA, OJY and IMN designed the data collection instruments, collected the data, and reviewed and revised the manuscript. MME, DAKT, OJY, JTN, CAM, JEN designed the study, coordinated, and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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