Prevalence and Utility of Low Mean Corpuscular Volume in Infants Admitted to the Neonatal Intensive Care Unit

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Objective To determine the prevalence of low mean corpuscular volume (MCV) in newborn infants admitted to the neonatal intensive care unit and to assess low MCV as a diagnostic test for alpha thalassemia.

Study design Retrospective analysis of all infants admitted to the neonatal intensive care unit between January 2010 and October 2018 for which a complete blood count was performed during the first 3 postnatal days. Infants with a low MCV were compared with those with a normal MCV. Infants with positive hemoglobin Bart (Hb Bart) were compared with those withnegative Hb Bart. Low MCV was also evaluated as a diagnostic test for alpha thalassemia.

Results A total of 3851 infants (1386 preterm, 2465 term) met the inclusion criteria and 853 (22.2%) had a low MCV. A low MCV was more common in term (25%) compared with preterm infants (17.1%, $P < .001$). Hb Bart positive newborn screening was identified in 133 infants (3.5%). Hb Bart was positive in 11.1% of infants with low MCV compared with 1.3% with normal MCV ($P < .001$). The sensitivity, specificity, positive predictive value, and negative predictive value of low MCV for the diagnosis of alpha thalassemia were 71.4%, 79.6%, 11.3%, and 98.7%, respectively.

Conclusions As Hb Bart positive newborn screens were seen in only 11.1% of infants with microcytosis, further diagnostic investigation may be warranted in individual infants. Further research to correlate microcytosis with iron status in infants and mothers is needed as well as studies using DNA analysis for the evaluation of alpha thalassemia variants. *(J Pediatr 2020;227:108-13)*.

Mean corpuscular volume (MCV) is one of the red blood cell (RBC) indices reported on a complete blood count (CBC). The MCV is used in children and adults to evaluate iron deficiency anemia, thalassemia, anemia of chronic disease, sideroblastic anemia, and lead toxicity.[1,2] Microcytosis (low MCV) in the neonatal period is defined as MCV <98 fL[3] for a full term infant. The most common causes of microcytosis in the neonatal population are alpha thalassemia and iron deficiency.[1,2]

Alpha thalassemia can be diagnosed by the presence of hemoglobin Bart (Hb Bart) on a routine newborn screening for hemoglobinopathy. However, newborn screening or testing for Hb Bart is not routinely performed or readily available in many countries where alpha thalassemia is common. Iron deficiency anemia is another possible cause for microcytosis in infants. Iron deficiency during pregnancy is common in the US and worldwide. Approximately 30%-50% of pregnant women are anemic, with iron deficiency as the most prevalent cause.[4,5] Moderate to severe iron deficiency anemia can deplete fetal iron stores.[5-8] Prematurity, small for gestational age (SGA), maternal diabetes, iron deficiency in prior pregnancy, shorter inter-gestational period, HIV, abnormal uterine bleeding, and in utero cigarette smoke exposure are risk factors for iron deficiency in infants.[9,10] Chronic fetal blood loss because of feto-maternal transfusion can also lead to iron deficiency in infants.[11,12]

MCV is underutilized in infants admitted to the neonatal intensive care unit (NICU). Previous studies have suggested that low MCV may be a simple way to detect alpha thalassemia.[13-18] Microcytosis can also be utilized to screen for iron deficiency in infants. The objectives of this study are to determine the prevalence and utility of monitoring low MCV in infants admitted to the NICU as well as to assess microcytosis as a diagnostic test for alpha thalassemia as determined by the presence of Hb Bart. We hypothesize that low MCV is common in infants admitted to the NICU and that infants with microcytosis are more likely to be positive for Hb Bart and, therefore, alpha thalassemia.

CBC	Complete blood count
Hb Bart	Hemoglobin Bart
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
NICU	Neonatal intensive care unit
PPV	Positive predictive value
RBC	Red blood cells
SGA	Small for gestational age

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Methods

This is a retrospective analysis of all infants admitted to the NICU at Thomas Jefferson University Hospital in Philadelphia, PA from January 2010 to October 2018, who had a CBC during the first 3 days after delivery. Infants who received a blood transfusion before the first CBC were excluded. The Institutional Review Board at Thomas Jefferson University Hospital approved this study.

Infants were identified from a neonatal database (Neodata, Isoprime Corporation, Lisle, Illinois; Neodata and Epic Systems, Verona, Wisconsin). For each infant, gestational age, birth weight, race, sex, and CBCs including hemoglobin, hematocrit, MCV, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width, and RBC count were collected. Pennsylvania newborn screening results were reviewed to determine the presence or absence of Hb Bart. The first CBC performed during the first 3 postnatal days was used for the analysis. The CBC samples were analyzed using Sysmex XE and Sysmex XN-9000 (Sysmex, Kobe, Japan). Statistical analysis was performed using the Sigma plot v 13 (Systat Software, Inc, Point Richmond, California) and the SPSS v 22 (IBM Corporation, Armonk, New York).

The primary outcome was the proportion of infants with low MCV. A low MCV was defined as <98 fL for infants born at ≥35 weeks of gestation, <99 fL for infants born between 29 and 34 weeks, <104 fL for infants born between 26 and 28 weeks, and <105 fL for infants born at ≤25 weeks of gestation.[3] Predetermined secondary outcomes were differences in hemoglobin and RBCs in preterm and term infants and in infants with low MCV and normal MCV. A similar comparison was performed between infants who were Hb Bart positive and Hb Bart negative. The predictive value of low MCV in determining a positive Hb Bart on newborn screening was also calculated. The groups were compared by Student *t* tests, Mann-Whitney U tests, or χ^2 tests as appropriate. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value were calculated. A logistic multivariable regression model was used for predicting microcytosis after adjusting for prematurity, African American race, male sex, SGA, exposure to cigarette smoking, and maternal diabetes. The receiver operating characteristics curve analysis was performed using a cut-off value of MCV for predicting positive Hb Bart. The difference was considered statistically significant for a 2-sided *P* value of <.05.

Results

A total of 4915 infants were admitted to the NICU during the study period, and a CBC was performed in 4281 infants (87.1%) during the first 3 postnatal days. Newborn screening results for Hb Bart were available for 3851 (90%) infants, and these infants were included in the analysis. MCV was low in 853 (22.2%) infants. Demographic characteristics and RBC indices are depicted in **Table I**. The newborn screening was positive for Hb Bart in a total of 133 (3.5%) infants. One infant with positive Hb Bart had severe anemia (Hb 7.8 mg/dL, MCV 77 fL) and was later diagnosed with Hb H disease (3 gamma globin gene deletion) by DNA analysis.

Thirty-six percent of infants were preterm (<37 weeks of gestation). MCV and MCH were lower in term infants than preterm infants, whereas hemoglobin, hematocrit, MCHC, and RBC count were lower in preterm infants (**Table II**). The incidence of microcytosis was higher in term infants compared with preterm infants, but more preterm infants were positive for Hb Bart. Infants with microcytosis had significantly lower hemoglobin concentration (**Table III**). MCH was lower and RBC count was higher in infants with low MCV. Infants with microcytosis were more likely to be positive for Hb Bart (11.1% vs 1.3%, $P < .001$). In infants with low MCV, the OR of a newborn screen positive for Hb Bart was 9.76 (95% CI, 9.38-10.15, $P < .001$). After adjusting for covariates, prematurity and SGA were associated with decreased odds of microcytosis, whereas African American race and male sex were associated with increased odds of microcytosis (**Table IV**; available at www.jpeds.com). Maternal diabetes or exposure to cigarette smoke was not predictive of microcytosis. The sensitivity, specificity, PPV, and negative predictive value of low MCV for the diagnosis of alpha thalassemia were 71.4%, 79.6%, 11.3%, and 98.7%, respectively (**Table V**; available at www.jpeds.com). The receiver operating characteristics curve analysis shows that a cut-off value of MCV <94 fL has 58% sensitivity and 92% specificity in predicting positive Hb Bart. Similarly, a cut-off value of MCV <100 fL has 72.2% sensitivity and 71.1% specificity (area under the curve = 0.8).

Infants who were positive for Hb Bart were compared with those negative for Hb Bart (**Table VI**; available at www.jpeds.com). Infants with positive Hb Bart had significantly lower MCV, MCH, MCHC, and higher RBC count and red cell

Table I. Demographics and CBC indices in the study population (mean ± SD) (n = 3851)

Birth weight (kg)	2.81 ± 0.91
Gestational age (wk)	37.7 ± 3.9
Preterm <37 wk (%)	1386 (36.0)
Race (%)	
African American	1407 (36.5)
Caucasian	890 (23.1)
Asian	323 (8.3)
Hispanic	158 (4.1)
Others	61 (1.6)
Unknown	1012 (26.3)
Male sex (%)	2084 (54.1)
Vaginal delivery (%)	2036 (52.9)
Hemoglobin (gm/dL)	16.8 ± 2.8
MCV (fL)	102 ± 7.6
MCH (pg)	35.6 ± 2.7
MCHC (gm/dL)	34.7 ± 1.2
RBC count (millions)	4.7 ± 0.8
RDW	17.1 ± 1.8
Infants with positive Hb Bart (%)	133 (3.5)

RDW, red cell distribution width.

Table II. Hemoglobin and RBC indices in preterm and term infants (mean ± SD) (n = 3851)

Variable	Preterm infants (n = 1386, 36%)	Term infants (2465, 64%)	OR (95% CI)	P
African American (%)	554 (40.0)	853 (34.6)	1.26 (1.12-1.39)	.001
Male sex (%)	728 (52.5)	1356 (55.4)	0.95 (0.90-1.02)	.15
SGA (%)	190 (13.7)	288 (11.7)	1.20 (1.00-1.40)	.08
Hemoglobin (gm/dL)	16.6 ± 3.0	16.9 ± 2.7		.002
Hematocrit (%)	47.9 ± 8.2	48.5 ± 7.2		.05
MCV (fL)	105 ± 8.5	101 ± 6.5		<.001
Low MCV (%)	237 (17.1)	616 (25.0)	0.62 (0.45-0.77)	<.001
MCH (pg)	36.4 ± 2.9	35.1 ± 2.4		<.001
MCHC (gm/dL)	34.6 ± 1.3	34.8 ± 1.2		<.001
RDW	17.2 ± 1.9	17.1 ± 1.7		.02
RBC count (millions)	4.6 ± 0.9	4.8 ± 0.7		<.001
Positive Hb Bart (%)	66 (4.8)	67 (2.7)	1.79 (1.44.2.14)	.001

distribution width. There were more African American infants who were positive for Hb Bart. Finally, infants who were Hb Bart positive were compared if they had normal or low MCV (Table VII). Hb was lower in infants who were Hb Bart positive with microcytosis.

Discussion

We report approximately 22% of infants admitted to the NICU have low MCV on a CBC performed within 3 days of birth. The newborn screening for Hb Bart was positive in 3.5% of infants admitted to the NICU. Hb Bart was more prevalent in preterm and African American infants. The infants with microcytosis were more likely to be positive for Hb Bart; however, 89% of infants with low MCV did not have a positive newborn screening for Hb Bart.

MCV is routinely used in adults and children to evaluate anemia, but this tool is underutilized in the NICU. Beta thalassemia, an important cause of microcytosis in adults and children, does not manifest during the neonatal period because of the absence of beta chains in fetal hemoglobin.[1,2] Lead poisoning and anemia of chronic infection are also extremely rare in infants.[1,2] The plausible explanations for low MCV in our cohort are iron deficiency and variants of alpha thalassemia not identified by the newborn screening for Hb Bart.

Congenital iron deficiency is important to recognize because a lack of iron during this critical period of brain development could lead to long-term neurodevelopmental problems.[19-22] Iron deficiency may occur if there is a maternal history of iron deficiency, utero-placental insufficiency, diabetes, cigarette smoking, obesity, and psychosocial stress.[5-9] Prematurity is also an important risk factor for iron deficiency, with up to 17% of premature infants reported to be iron deficient at birth.[23] The prevalence of microcytosis and possible iron deficiency is much higher in our cohort than reported by others. As per the normative data from a study by Christensen et al, only 2.5% of infants (<2 SD) had low MCV.[3] However, the infants included in that study were healthy term infants. In a study by MacQueen et al, 16 of 180 (8.9%) high-risk infants (infant of mothers with diabetes, SGA, and very low birth weight) had laboratory evidence of iron deficiency at birth.[24] Only 2 of 16 infants with laboratory evidence of iron deficiency had microcytosis.[24] The prevalence of microcytosis was high in our cohort, most likely because of the inclusion of preterm and sick term infants admitted to the NICU who have a higher risk of iron deficiency. A study from China found that 45% of infants born to mothers with iron deficiency were iron deficient at birth despite oral supplementation of daily iron during pregnancy.[25]

An alternative explanation for microcytosis in our cohort includes cases of heterozygous alpha thalassemia not

Table III. Comparison of neonates with normal MCV and low MCV (mean ± SD)

Variable	Low MCV (n = 853)	Normal MCV (n = 2998)	OR (95% CI)	P
Preterm <37 wk (%)	237 (27.8)	1149 (38.3)	0.62 (0.45-0.79)	<.001
African American race (%)	394 (46.2)	1013 (33.8)	1.68 (1.53-1.83)	<.001
Male sex (%)	507 (59.4)	1577 (52.6)	1.32 (1.17-1.47)	<.001
Smoking exposure (%)	93 (10.9)	341 (11.4)	0.95 (0.71-1.20)	.7
SGA (%)	84 (9.8)	394 (13.1)	0.72 (0.47-0.97)	.01
Infants of diabetic mothers (%)	98 (11.5)	314 (10.5)	1.11 (0.87-1.35)	.4
Hemoglobin (gm/dL)	16.2 ± 2.8	17.0 ± 2.8		<.001
MCV (fL)	93 ± 4.9	105 ± 5.9		<.001
MCH (pg)	32.3 ± 2.3	36.5 ± 2.0		<.001
MCHC (gm/dL)	34.8 ± 1.3	34.7 ± 1.2		.4
RBC count (millions)	5.0 ± 0.8	4.7 ± 0.8		<.001
RDW (%)	17.1 ± 2.0	17.2 ± 1.7		.2
Infants with positive Hb Bart (%)	95 (11.1)	38 (1.3)	9.76 (9.38-10.15)	<.001

Table VII. Comparison of infants with Hb Bart positive with normal and low MCV (median, IQR)

Variable	Hb Bart positive Low MCV (n = 96)	Hb Bart positive Normal MCV (n = 37)	OR (95% CI)	P
Preterm <37 wk (%)	45 (46.9)	22 (59.5)	0.60 (−0.18 to 1.37)	.3
Black race (%)	49 (52.8)	23 (62.2)	0.63 (−0.14 to 1.41)	.3
Male sex (%)	54 (56.2)	20 (54.1)	1.09 (0.33-1.85)	1.0
Hemoglobin (gm/dL)	15.8 ± 2.7	17.7 ± 2.8		<.001
MCV (fL)	88 ± 6.3	104 ± 3.9		<.001
MCH (pg)	29.5 ± 2.5	35.0 ± 2.0		<.001
MCHC (gm/dL)	33.5 ± 1.2	33.7 ± 1.4		.4
RBC count (millions)	5.4 ± 0.8	5.0 ± 0.8		.05
RDW (%)	18.2 ± 2.2	17.8 ± 2.2		.4

identified on newborn screening for Hb Bart. DNA based studies have shown that a substantial number of heterozygous alpha thalassemia are missed if Hb Bart at birth is used for the screening of alpha thalassemia.[26,27] Fetal hemoglobin has 2 alpha and 2 gamma globin chains. The defective production of alpha chains in the fetus is reflected by the presence of tetramers of gamma chains called Hb Bart. Alpha thalassemia is caused by a deletion or mutation in one or more of the 4 genes coding for alpha globin.[26] The severity of alpha thalassemia depends on the number of genes affected. Microcytosis without anemia is seen with 1 gene (silent carrier) or 2 gene deletion (trait). Three-gene deletion manifests with moderate to severe anemia (Hb H disease) and 4-gene deletion is lethal and leads to hydrops fetalis.[26,28] An early diagnosis of alpha thalassemia in the neonatal period may prevent further diagnostic workup and unnecessary interventions, such as iron supplementation when microcytosis is found on a screening CBC later in life. The infant's silent carrier or trait status is also important for genetic counseling for parental family planning as well as for the patient's own reproductive years. In the US, alpha thalassemia can be diagnosed on hemoglobinopathy testing performed for routine newborn screening. In our cohort, 3.5% of infants were positive for Hb Bart. Approximately 5% of the population worldwide carry an alpha thalassemia variant.[26] Alpha thalassemia is a common gene defect in Southeast Asia as well as populations originating from the Mediterranean, Central Asia, the Middle East, and Africa.[26] However, routine newborn screening for hemoglobinopathy is unavailable in a majority of the countries where alpha thalassemia is prevalent. In countries where newborn screening for Hb Bart is not readily available, low MCV is used for the screening of alpha thalassemia. Several studies report that low MCV at birth is an acceptable screening tool for the diagnosis alpha thalassemia.[14,15,17,18] We report that the sensitivity and PPV of microcytosis for identifying infants with alpha-thalassemia is low in our cohort. Only 11% of infants with low MCV were positive for Hb Bart. Although, it has been reported that Hb Bart at birth is a sensitive indicator of the presence of alpha thalassemia variant, DNA-based studies showed that this diagnostic method may miss cases of alpha thalassemia trait.[26,29-31] It is possible that using Hb Bart to diagnose alpha thalassemia underestimates the true frequency of the alpha thalassemia trait in our population. Conversely, 29% of infants with Hb Bart had a normal MCV in our cohort. It is likely that infants with Hb Bart with normal MCV are silent carriers with loss of only 1 gene. There were more preterm than term infants in our cohort who were positive for Hb Bart, and among infants positive for Hb Bart, preterm infants were more likely to have a normal MCV. Hb Bart in preterm infants with normal MCVs may reflect normal transition from Hb Bart to fetal Hb. The percent of Hb Bart in cord blood correlates with the number of alpha globin defective genes and a Hb Bart level at 0.2% can be used as a cut-off point for the diagnosis of alpha thalassemia with a diagnostic efficiency of 97.6%.[30] Unfortunately, the Pennsylvania State newborn screening only reports presence or absence of Hb Bart, not the actual percentage of Hb Bart.

Iron deficiency is another explanation for microcytosis in our cohort. Congenital iron deficiency or iron deficiency during early infancy are associated with long-term adverse neurocognitive, sensory, and behavioral consequences.[19-22] Placental transfusion with delayed cord clamping and umbilical cord milking can improve iron stores and prevent iron deficiency.[32,33] Similarly, supplementation of iron immediately after birth will improve iron stores and prevent anemia. However, in animal models of fetal and neonatal iron deficiency, iron supplementation corrects the anemia but does not reverse the neurocognitive deficits that occur due to lack of iron during critical periods of brain development in fetal life.[22,34-37] In children identified as iron deficient at 6, 12, and 18 months of age, iron supplementation failed to improve cognitive function at 10 years of age.[38] During acute or chronic fetal hypoxia, iron utilization in the fetus is directed toward RBC production at the expense of the brain and other organs.[39] Low MCV in our cohort likely represents more severe and longer periods of iron deficiency in the fetus. Early recognition of the fetus at risk for iron deficiency and maternal iron supplementation or blood transfusion during early pregnancy may help in preventing long-term consequences of fetal and neonatal iron deficiency.[5] A study from a high-income country reported that microcytosis, not the current diagnostic criteria for iron deficiency (serum iron and ferritin), was associated with lower cognitive outcomes at 2 years in a healthy cohort of young children.[40] It is possible that microcytosis is a better predictor of neurodevelopmental outcomes as it indicates more severe and chronic iron deficiency than a one-time measurement of serum iron and ferritin.

Infants of mothers with diabetes, SGA infants, very low birth weight premature infants, and infants exposed to in utero cigarette smoke are at increased risk for developing iron deficiency at birth.[5,9,24] In our cohort, the number of infants with microcytosis was lower in preterm infants compared with term infants. Similarly, rates of microcytosis were not increased in infants of diabetic mothers or infants with in utero cigarette smoke exposure. Surprisingly, the proportion of infants with microcytosis was lower for SGA infants in our cohort. We did not obtain laboratory evidence of iron deficiency, and it is possible that infants with high risk for congenital iron deficiency in our cohort may have a milder form of iron deficiency with normal erythropoiesis.

The strength of our study is the large sample size of infants admitted to the NICU and the data included from the CBC performed within 72 hours of age, which reflects fetal erythropoiesis. We recognize several limitations to our study. It was performed retrospectively at a single center, and a number of infants were excluded due to unavailability of newborn screening results or a CBC that was not performed within 72 hours after birth. We have no data on the status of iron in infants and mothers. However, other studies have shown microcytosis is a better indicator of cognitive outcomes than serum iron or ferritin levels.[37] In addition, Pennsylvania state newborn screening only reports the presence or absence of Hb Bart. Because the percentage of Hb Bart is not reported, there is limited ability to correlate the severity of alpha thalassemia with low MCV.

In our study, approximately 22% of infants admitted to the NICU had low MCVs on CBCs performed within 3 days after birth. The infants with microcytosis were more likely to be positive for Hb Bart but approximately 89% of infants with low MCV did not have a positive newborn screening for Hb Bart suggesting an alternative cause for microcytosis. Further research is warranted to correlate microcytosis with iron status in infants and mothers, to perform DNA analysis for alpha thalassemia variants, and to study long-term cognitive outcomes in infants with microcytosis without alpha thalassemia. Ultimately this may lead to the prevention of microcytosis at birth by optimizing efficient iron supplementation to high risk mothers. ■

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50 Years Ago in *The Journal of Pediatrics*

The Changing Landscape of Iron Deficiency Diagnosis

Hogan GR, Jones B. The relationship of koilonycbia and iron deficiency in infants. J Pediatr 1970;77:1054-7.

Fifty years ago in *The Journal,* Drs Jones and Hogan documented the prevalence of koilonychia, a form of concave nail dystrophy, in an infant population and evaluated its association with iron deficiency. Age-matched controls were used to compare iron studies, including serum iron and hemoglobin. The authors found significantly lower than normal serum iron and hemoglobin levels in the 5% of infants with koilonychia and reported a correlation between koilonychia and iron deficiency in a pediatric population.

Our understanding of koilonychia has not changed significantly over the past 50 years, and the etiology remains poorly understood. Vasculopathy, endocrinopathies, nutritional deficiencies, and trauma may play roles.[1] In children, koilonychia is generally considered idiopathic; however, the literature suggests that nutritional deficiencies should be considered.[1] Although our understanding of koilonychia is limited, our insight into iron homeostasis and iron deficiency has expanded. According to Hogan and Jones, "serum iron concentration is the most easily available valid laboratory method for proving the depletion of iron stores." Two years after this publication, the serum ferritin assay, a critical component of our current iron deficiency workup, was developed. Although ferritin was discovered in the 1930s, a reliable assay did not become available until 1972. A low ferritin level is highly specific for iron deficiency; however, interpretation of normal or high ferritin levels can be difficult because the protein functions as an acute phase reactant. Other iron status markers, such as soluble transferrin receptor and total iron-binding capacity, are important diagnostic tools. Serum iron levels can be affected by recent dietary intake and is less reliable for diagnosis.

Iron deficiency is seen in 8%-14% of children and is associated with neurocognitive impairment. An exam finding of koilonychia would still prompt testing for iron deficiency, but our screening, diagnostic testing, and subsequent treatment of this condition has improved substantially over the decades. Because iron is a critical component of health outcomes in young children, we suspect that the breadth of knowledge will continue to evolve rapidly throughout the next 50 years.

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Table IV. Multivariable regression analysis to predict microcytosis

Variable	OR (95 CI)	*P*
Prematurity	0.60 (0.51-0.71)	<.001
Male sex	1.29 (1.11-1.51)	.001
African American race	1.73 (1.48-2.02)	<.001
Infants of mothers with diabetes	1.09 (0.86-1.40)	.47
Small for gestation age	0.77 (0.60-1.00)	.046
Cigarette smoke exposure	1.10 (0.86-1.410	.46

Table V. Diagnostic test evaluation for identifying infants with alpha thalassemia using low MCV (n = 3851)

Variable	Hb Bart positive (95% CI)	Hb Bart negative (95% CI)
Low MCV	95	758
Normal MCV	38	2960
Sensitivity (%)	71.4 (62.9-78.9)	
Specificity (%)	79.6 (78.3-80.9)	
PPV (%)	11.3 (10.1-12.6)	
NPV (%)	98.7 (98.3-99.0)	
Likelihood ratio for positive test (LR+)	3.5 (3.1-4.0)	
Likelihood ratio for negative test (LR-)	0.36 (0.27-0.47)	

NPV, negative predictive value

Table VI. Comparison of neonates negative and positive for Hb Bart (median, IQR)

Variable	Hb Bart positive (n = 133)	Hb Bart negative (n = 3718)	OR (95% CI)	*P*
Preterm <37 wk (%)	66 (49.6)	1463 (38.0)	1.53 (1.19-1.88)	.02
African American race (%)	72 (54.1)	1335 (35.9)	2.11 (1.76-2.45)	<.001
Male sex (%)	74 (59)	2010 (54.1)	0.83 (0.48-1.18)	.8
Hemoglobin (gm/dL)	16.3 ± 2.8	16.8 ± 2.8		.04
MCV (fL)	92.5 ± 9.2	103 ± 7.3		<.001
Number of infants with low MCV (%)	96 (72.2)	757 (20.4)	10.15 (9.76-10.54)	<.001
MCH (pg)	31.0 ± 3.4	35.7 ± 2.5		<.001
MCHC (gm/dL)	33.5 ± 1.2	34.8 ± 1.2		<.001
RBC count (millions)	5.3 ± 0.8	4.7 ± 0.8		<.001
RDW (%)	18.1 ± 2.2	17.1 ± 1.8		<.001