Severe Anemia at Birth—Incidence and Implications

Timothy M. Bahr, MD[1,2], Shelley M. Lawrence, MD[2], Erick Henry, MPH[1], Robin K. Ohls, MD[2], Shihao Li, MS[1], and Robert D. Christensen, MD[1,2]

Objective To identify neonates with severe anemia at birth, defined by a hemoglobin or hematocrit value within the first 6 hours after birth that plotted below the 1st percentile according to gestational age. For each patient, we retrospectively determined whether caregivers recognized the anemia within the first 24 hours after birth and the probable cause and outcome of anemia.

Study design This was a retrospective cohort analysis of Intermountain Healthcare population-based data from neonates born between January 2011 and December 2020 who had a hemoglobin or hematocrit value measured within the first 6 hours after birth below the 1st percentile lower reference interval (hematocrit ~35% in near-term/term neonates).

Result Among 299 927 live births, we identified 344 neonates with severe anemia at birth. In 191 of these neonates (55.5%), the anemia was recognized by caregivers during the first 24 hours. Anemia was more likely to be recorded as a problem (85%) if the hemoglobin was ≥2 g/dL below the 1st percentile ($P < .001$). The lowest hemoglobin values occurred in those in whom hemorrhage was the probable cause ($P < .013$ vs hemolysis and $P < .001$ vs hypoproduction, mixed cause, or indeterminant.) Treatment was provided to 39.5%. A retrospective review suggested that mixed mechanisms, particularly hemorrhagic plus hemolytic, occurred more commonly than was recognized at the time of occurrence.

Conclusions Severe anemia at birth often went unrecognized on the first day of life. Algorithm-directed retrospective reviews commonly identified causes that were not listed in the medical record. We postulate that earlier recognition and more accurate diagnoses would be facilitated by an electronic medical record–associated hemoglobin/hematocrit gestational age nomogram. *(J Pediatr 2022;248:39-45)*.

Anemia is consequential, often resulting in reduced physical capacity and performance, yet it can generally be effectively treated, once it has been diagnosed and its cause accurately characterized.[1] During the transition from fetus to neonate, anemia can be particularly detrimental. A practical definition of neonatal anemia that our health care system has used since 2009 is a hemoglobin or hematocrit value below the 5th percentile lower reference interval for gestational and postnatal age.[2] It is important that neonatal anemia is diagnosed according to gestational and postnatal age reference intervals, because hemoglobin and hematocrit values increase almost linearly from 22 to 40 weeks of gestation.[2-4] Anemia at birth, whether due to hemorrhage, hemolysis, hypoproduction, or combinations of these issues, can result in significant morbidity or death.[5-7] Timely treatment of severe anemia can restore the perfusion necessary for adequate organ function.[8]

None of our previous neonatal complete blood count (CBC) reference interval publications focused on severe anemia at birth. Moreover, we recognize that some newborn infants with a low hemoglobin or hematocrit, defined as <5th percentile, are asymptomatic and may not need diagnostic evaluation or treatment.[3] Consequently, we examined the possibility of defining severe anemia at birth by a hemoglobin/hematocrit below the 1st percentile lower reference interval for gestational age, using the large Enterprise Data Warehouse at Intermountain Healthcare. To evaluate this definition of severe anemia at birth, we examined the records of all neonates in our health care system during the past 10 years (2011-2020) who met this criterion.

Focusing on neonates with an hematocrit or hemoglobin, during the first 6 hours after birth, which plotted below the first percentile, we sought to determine the proportion of these neonates who were recognized (ie, diagnosed) by the health care team as being anemic on the first day (a note listing anemia, or anemia treatment, anywhere in the medical record), the probable cause of the anemia (using an algorithm to assign cause[3]), associations between the cause and severity of anemia, treatments given, and the proportion of cases in which our research team retrospectively identified a cause of the anemia that was not listed in the medical record or identified a cause in addition to the one listed.

CBC	Complete blood count
DIC	Disseminated intravascular coagulation
EMR	Electronic medical record
NICU	Neonatal intensive care unit

From the From [1]Obstetric and Neonatal Operations, Intermountain Healthcare, Salt Lake City, UT; and [2]Division of Neonatology, Department of Pediatrics, University of Utah Health, Salt Lake City, UT

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Methods

The study protocol was approved by the Intermountain Healthcare Institutional Review Board with a waiver of informed consent because this was a deidentified, data-only study with appropriate privacy protection. Intermountain Healthcare is a not-for-profit health care system operating 18 hospitals with labor and delivery units in Utah and Idaho. Data from neonates born between January 1, 2011, and December 31, 2020, were obtained from the Intermountain Healthcare data warehouse by authorized Intermountain data analysts.

We began the analysis by determining the 1st percentile hemoglobin/hematocrit values by gestational age, using a database of >350 000 CBCs obtained on the day of birth.[4] We then identified all neonates in our database during the past 10 years with a hemoglobin/hematocrit drawn during the first 6 hours after birth that fell below the 1st percentile.

All blood tests were performed in accordance with Intermountain Healthcare Laboratory Services standard operating procedures and manufacturer's instructions. Sysmex quality control procedures were performed daily in each hospital clinical laboratory, as recommended by the manufacturer (Sysmex America).

We constructed the hemoglobin and hematocrit reference interval from >350 000 individual CBC tests of blood specimens drawn on the day of birth. The source of the blood specimen (infant vein, capillary, or artery or placenta/umbilical cord) was recorded. Neonates who had received a prenatal or postnatal red blood cell transfusion at any time before the CBC was drawn were excluded from the reference interval data set, as were all those with a diagnosis of a chromosomal abnormality. The gestational age of each subject in the reference interval data set was derived from the neonatal records. The reference interval chart displaying the 5th, median, and 95th reference intervals for hemoglobin and hematocrit on the day of birth was published previously.[4] Using those data, we began the present study by calculating the 1st percentile reference interval according to gestational age as our means of defining severe anemia at birth (**Figure 1**).

Data for infants with a hemoglobin or hematocrit value drawn within the first 6 hours after birth that fell below the 1st percentile for gestational age were transferred into a REDCap (Research Electronic Data Capture) database for further investigation and analysis. Researchers reviewing the electronic medical record (EMR) for neonates with severe anemia at birth reviewed all provider notes and problem lists from the first 24 hours of life and recorded whether recognition of the anemia was documented by providers in their notes or a treatment for anemia was provided. We did not rely on coding for diagnoses or recognition of anemia but rather obtained all such information directly from individual medical records.

In addition, the researchers attempted to categorize the cause of the anemia according to the algorithm shown in **Figure 2** (available at www.jpeds.com). Specific criteria were used to categorize the anemia as the result of hemorrhage, hemolysis, hypoproduction, or a combination of these etiologies. When the available data were insufficient to justify a classification, researchers selected the category "unable to determine the cause." Owing to the descriptive nature of the study, data analysis consisted primarily of summaries. Continuous variables were summarized with means and compared across groups using the *t* test. Categorical variables were summarized with counts and percentages and were compared across groups using the Fisher exact test. All statistical analyses and data manipulation were done using the R statistical language and environment (R Foundation for Statistical Computing).

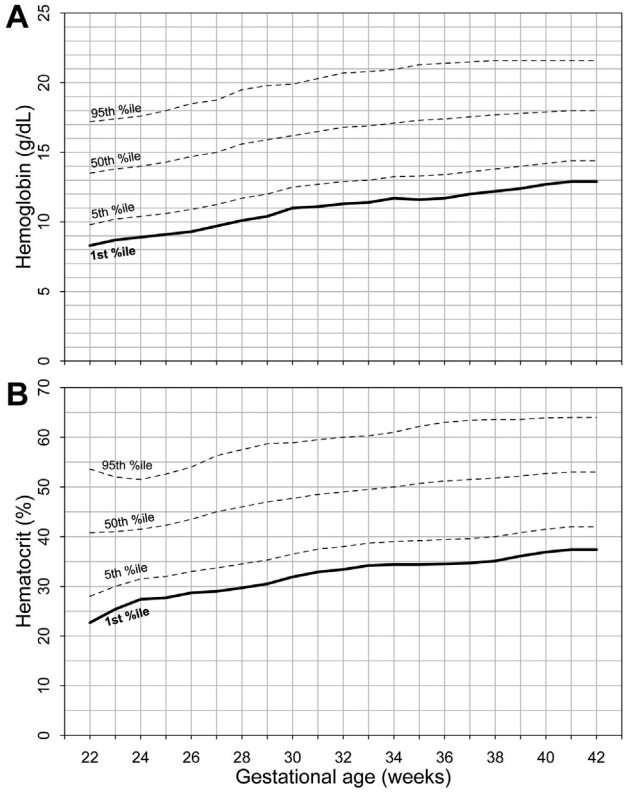

Figure 1. Reference intervals for **A,** hemoglobin and **B,** hematocrit of neonates on the day of birth, according to their gestational age. The dark bold line indicates the 1st percentile lower reference interval, below which (for the purpose of this study) a neonate is considered to have severe anemia at birth. The dashed lines show the 5th percentile, the median, and the 95th percentile reference intervals as labeled.

Results

During the 10-year study period, 299 927 live births were recorded at the Intermountain Healthcare hospitals, with the following ethnic/racial distribution: White, 90.6%; Black or African American, 1.5%; American Indian and Alaska Native, 1.6%; Asian, 2.7%; Native Hawaiian and Other Pacific

Table I. Demographic, laboratory, and outcome features of 344 neonates over the past 10 years meeting our definition of severe anemia at birth

Features	Anemia was recognized on the first day (N = 191)	Anemia was present but not recognized on the first day (N = 153)	*P* value
Gestational age, wk, mean ± SD	35.1 ± 4.1	36.1 ± 3.4	.018
Birth weight, g, mean ± SD	2511 ± 934	2680 ± 897	.091
Lived, n (%)	168 (88.0)	140 (91.5)	.373
Initial hemoglobin, g/dL, mean ± SD*	9.1 ± 2.6	11.2 ± 1.4	<.001
Initial hematocrit, %, mean ± SD*	27.9 ± 6.8	34.1 ± 4.4	<.001
Probable cause hemorrhage, n (%)†	72 (37.7)	25 (16.3)	<.001
Probable cause hemolysis, n (%)†	36 (18.8)	5 (3.3)	
Probable cause hypoproduction, n (%)†	5 (2.6)	0 (0.0)	
Probable cause mixed mechanisms, n (%)†	30 (15.7)	3 (2.0)	
Unable to determine probable cause, n (%)†	48 (25.1)	120 (78.4)	

Two groups are compared, those in whom a note in the medical record within 24 hours of birth identified anemia as a problem and those in who anemia was present but not recorded during the first day.
*There was 1 missing hemoglobin value in the "anemia was recognized on the first day" group. There were no other missing hemoglobin or hematocrit values.
†Probable cause of the anemia was determined by the researchers after studying the laboratory and clinical data and the clinical record (see Figure 2).

Islander, 1.1%; 2 or more races, 2.6%; Hispanic or Latino, 14.4%; White not Hispanic or Latino, 77.8%.

Of the almost 300 000 live births in our records, 76 415 neonates had a hemoglobin/hematocrit value drawn within the first 6 hours following birth, and 355 had a value <1st percentile lower reference interval. We identified 11 of the 355 cases in which we judged the initial hemoglobin/hematocrit value to be incorrect because a repeat hemoglobin/hematocrit drawn within 1 hour and prior to transfusion was normal (ie, within the reference interval for gestational age[4]). Perhaps these were the result of phlebotomy techniques (eg, drawn from an intravenous line with fluid contamination and sample dilution or blood clotting within the microtube) or a laboratory error, because an immediate redraw was normal (within the reference interval). Thus, the total number of neonates with severe anemia at birth used for final analysis was 344. One hundred forty-three (41.6%) of these hemoglobin/hematocrit values were obtained from a placenta or umbilical cord blood specimen, and the remaining 201 values (58.4%) were obtained from specimens drawn from a neonate.

Demographic, laboratory, and outcome measures of the 344 neonates are shown in Table I. The 191 infants (55.5%) who were recognized (ie, recorded by the health care team) to have severe anemia during the first day were of slightly lower gestational age and had lower hemoglobin and hematocrit values compared with the 153 infants (44.5%) with anemia that initially went unrecognized. The distribution of anemia cases across probable causes differed between those cases in which anemia was recognized on the first day and those in which anemia was initially unrecognized. Anemia due to either hemorrhage or hemolysis was likely to be recognized early; however, among infants in whom no cause of the anemia was ever identified, either at the time of occurrence or during the retrospective review process, 71.4% of cases went unrecognized during the first day. In contrast, in those whose cause of anemia was identified, only 14.7% of cases went unrecognized during the first day.

Thirty-six of the 344 neonates with severe anemia at birth died prior to discharge (10.5%). A greater proportion of neonates died prior to discharge in the group in which anemia was recognized on the first day of life (23 of 191; 12.0%) compared with the unrecognized group (13 of 153; 8.5%), but this difference was not statistically significant ($P = .373$) (Table I). Demographic, laboratory, and outcome measures of the 344 neonates, stratified by survival to discharge, are displayed in Table II. Compared with the neonates who survived to discharge, the 36 neonates who died prior to discharge were

Table II. Demographic and laboratory features, and probable causes of anemia among 344 neonates during the past 10 years, each of whom met the definition of severe anemia at birth, stratified by survival to discharge

Features	Died prior to discharge (N = 36)	Survived through discharge (N = 308)	*P* value
Gestational age, wk, mean ± SD	33.0 ± 5.3	35.8 ± 3.5	.004
Birth weight, g, mean ± SD	2045 ± 1238	2648 ± 858	.008
Initial hemoglobin, g/dL, mean ± SD*	8.7 ± 2.9	10.2 ± 2.3	.005
Initial hematocrit, %, mean ± SD*	28.0 ± 8.0	31.0 ± 6.3	.034
Probable cause hemorrhage, n (%)†	12 (25.8)	85 (27.6)	.024
Probable cause hemolysis, n (%)†	2 (5.6)	39 (12.7)	
Probable cause hypoproduction, n (%)†	2 (5.6)	3 (1.0)	
Probable cause mixed mechanisms, n (%)†	7 (19.4)	26 (8.4)	
Unable to determine probable cause, n (%)†	13 (36.1)	155 (50.3)	

*There was 1 missing hemoglobin value in the "survived through discharge" group. There were no other missing hemoglobin or hematocrit values.
†Probable cause of the anemia was determined by the researchers after studying the laboratory and clinical data and the clinical record (see Figure 2).

more likely to be born at an earlier gestational age, to have a lower birth weight, and to have lower first hemoglobin or hematocrit measurements (all $P < .01$). In addition, those who died prior to discharge were more likely to have hypoproduction or mixed mechanisms as the probable cause of anemia and less likely to have hemolysis as the probable cause. A probable cause of anemia was determined in a greater proportion of neonates who died prior to discharge compared with those who survived through discharge.

Table III displays information from the group of 176 neonates who had at least 1 probable cause of their anemia identified. Hemorrhage was the leading cause, followed by hemolysis, with hypoproductive conditions the least common cause. In the 129 neonates with hemorrhagic anemia, fetal bleeding with a perinatal event (such as abruption) and fetomaternal hemorrhage were the most common causes. These conditions were likely to be recognized on the first day. Of those infants with hemolytic anemia, immune-mediated hemolysis was more common than nonimmune hemolysis, with disseminated intravascular coagulation (DIC) the predominant nonimmune hemolytic anemia. Immune-mediated hemolytic anemia caused by Rh D alloimmunization was more likely than other immune causes to be recognized within the first day. Two infants were eventually diagnosed with Diamond Blackfan anemia, 3 others had other congenital syndromes, and 3 did not have a recognized syndrome; 1 of the latter group had severe congenital iron deficiency. A diagram illustrating the distribution of cases by probable cause is shown in Figure 3 (available at www.jpeds.com).

In some instances, the medical record did not list a probable cause of anemia, but our research team retrospectively assigned a probable cause. In other cases, our team identified a cause in addition to the cause listed in the medical record (Table IV; available at www.jpeds.com). We were more likely to retrospectively identify instances of multiple causes, particularly the combination of hemorrhage and hemolysis. The most common instances in which no cause was listed in the medical record but the research team identified a probable cause involved fetomaternal hemorrhage. Some of those neonates had no Kleihauer–Betke testing, but had elevated mean corpuscular volume, red blood cell distribution width, and nucleated red blood cell count values in the absence of any other explanation for anemia.[9] Others who had no cause listed in the medical record but did have a cause identified by the research team had DIC, documented by D-dimers, hypofibrinogenemia, elevated prothrombin time and activated thromboplastin time, low or falling platelet count, and schistocytosis.[10,11]

For each case, we quantified the severity of the anemia using the metric grams per deciliter of hemoglobin below the 1st percentile lower reference interval for gestational age. Thus, the lower the hemoglobin in relationship to the 1st percentile line, the more severe the anemia. A relationship between anemia severity and cause is shown in Figure 4. The least severe cases were the most likely to have no cause identified. The most severe cases were likely to be hemorrhagic.

Discussion

Anemia at birth can result from a wide variety of causes and can be chronic or acute.[12,13] Because of these variables, it is useful not only to identify anemia at birth, but also to attempt to find its cause, assess the patient for signs of physiologic compromise, and determine whether treatment is indicated.

Table III. Probable causes of severe anemia at birth among the group of 176 neonates where one or more cause(s) was identified

Probable causes*	Number (N = 207)	Anemia was recognized on the first day, n (%)	Anemia was present but not recognized on the first day, n (%)	*P* value
Hemorrhage (N = 129)				
Fetal bleeding with abruption or other perinatal event	48	36 (75.0)	12 (25.0)	<.001
Fetomaternal	44	37 (84.0)	7 (16.0)	<.001
Twin-twin transfusion syndrome	15	10 (66.7)	5 (33.3)	.302
Fetal internal bleeding (not subgaleal)	10	7 (70.0)	3 (30.0)	.343
Subgaleal hemorrhage	3	3 (100.0)	0	ND
Other	9	8 (88.9)	1 (11.1)	.046
Hemolysis (n = 73)				
Immune: Rh D	15	15 (100.0)	0	<.001
Immune: Rh C, c, E, e	10	8 (80.0)	2 (20.0)	.114
Immune: other	14	11 (78.6)	3 (21.4)	.061
Nonimmune: DIC	27	24 (88.9)	3 (11.1)	<.001
Nonimmune: other†	7	6 (85.7)	1 (14.3)	.131
Hypoproduction (n = 8)				
Diamond–Blackfan anemia	2	2 (100.0)	0	ND
Other syndromic	3	3 (100.0)	0	ND
Other nonsyndromic	3	3 (100.0)	0	ND

ND, statistical hypothesis test not done owing to small sample size, limiting the validity of statistical inference.
The total number with a cause assigned is 207, because some had more than 1 cause identified.
*"Probable cause" of the anemia was determined by the researchers studying the laboratory and clinical data and the clinical record (see Figure 2).
†The cases of "hemolysis, nonimmune, other" included hereditary spherocytosis (n = 4), alpha thalassemia (2 gene deletions) plus hereditary pyropokilocytosis (n = 2), and congenital dyserythropoietic anemia type I (n = 1).

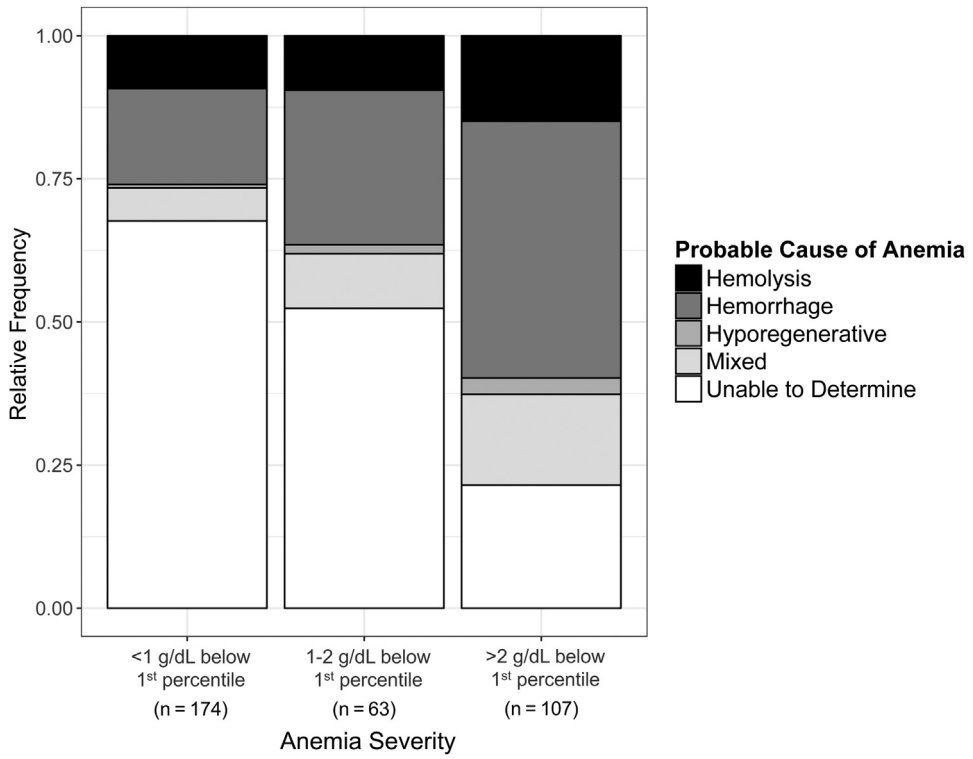

Figure 4. The relationship between the probable cause of anemia and severity of anemia. The probable cause among 344 cases was categorized as hemolysis, hemorrhage, hypoproduction, mixed, or unable to determine. Severity was quantified using the metric hemoglobin (Hgb; g/dL) below the 1st percentile lower reference interval for gestational age. In the bar graph, severity is clustered into 3 groups; least severe Hgb was <1 g/dL below the 1st percentile; medium severity Hgb was 1-2 g/dL below the 1st percentile, and the most severe Hgb was >2 g/dL below the 1st percentile for gestational age.

In neonatal hematology, we generally diagnose any CBC value as being abnormal if it is either below the 5th percentile lower reference interval or above the 95th percentile upper reference interval.[12] Using this standard practice, 5% of all neonates who have a CBC may be labeled as anemic, although certainly not all such neonates are symptomatic or in need of treatment.[3] Although the 5th percentile designation method has merit, in this study we sought to define a more medically significant subset of anemic neonates. We accomplished this by identifying those with hemoglobin/hematocrit values during the first 6 hours after birth that charted below the 1st percentile according to their gestational age (**Figure 1**).

As we studied the records of 344 neonates who met our definition for severe anemia at birth, we were somewhat surprised to find that 45% of them did not have anemia recognized by the health care team until after 24 hours (or at least there was no mention of anemia in the medical record). Infants most likely to be recognized early had extremely low hemoglobin values, specifically those with a hemoglobin value ≥ 2 g/dL below the 1st percentile line. The majority of those neonates had hemorrhagic anemia. We hypothesize that if our clinicians would have had a 1st percentile nomogram readily available, perhaps as part of the EMR or an alert in the laboratory section of the EMR, they would have promptly recognized these 344 patients as being anemic at birth.

In a study from Porto, Portugal, Rocha et al compared 34 neonates with anemia (mean hemoglobin 12.8 ± 1.5 g/dL) at admission to the neonatal intensive care unit (NICU) and 72 neonates without anemia (mean hemoglobin 16.8 ± 2.1 g/dL; $P < .001$).[14] The anemic group was of slightly lower mean gestational age (26 ± 2 weeks vs 27 ± 2 weeks; $P = .025$), was more likely to receive inotropic support (52.9% vs 31.9%; $P = .041$), and had a longer duration of mechanical ventilation (9 days vs 2 days; $P = .012$), more frequent hemodynamically significant patent ductus arteriosus (64.7% vs 41.7%; $P = .006$), and severe intraventricular hemorrhage (41.2% vs 16.7%; $P = .005$). However, it was unclear whether the anemia was the proximate cause of their more severe clinical illness. In addition, these patients had hemoglobin levels considerably higher than those that we report here.

Tao et al from Hangzhou, China, reported 8 cases of severe anemia at birth among 6825 neonates admitted to their neonatal unit.[15] All cases were the result of fetomaternal hemorrhage, and all neonates presented with pallor but without hydrops, with hemoglobin levels ranging from 2.5 to 5.3 g/dL. Although 3 mothers reported decreased fetal movement, only 1 (with the lowest hemoglobin) underwent a sinusoidal fetal heart rate tracing. All neonates were discharged home after a hospital stay ranging from 5 to 12 days. This group used 6 g/dL as the hemoglobin cutoff

for severe anemia at birth regardless of gestational age, but they did not explain their rationale for this cutoff. Based on our data, 6 g/dL is well below the 1st percentile for all gestational ages and limited the number of cases included in their study.

In a publication related to severe anemia in utero, Mizuuchi et al from Sapporo, Japan reported a nationwide survey of 100 intrauterine transfusions performed mainly for red cell alloimmunization, anemic donors of twin–twin transfusions, and parvovirus B19 infection.[16] Similarly, we found red cell alloimmunization to be the most common cause of hemolytic anemia at birth. However, we also identified DIC as a leading cause of hemolysis, with many such cases occurring concomitantly with hemorrhagic anemia. Also similar to the Sapporo report, donors of twin–twin transfusions were a leading cause of hemorrhagic anemia in our analysis. However, unlike the survey from Japan, we identified no cases of red cell hypoproduction at birth resulting from parvovirus B19 infection. Perhaps some such cases did exist in our data set but were undiagnosed in neonates with no identified cause for their anemia.

We recognize several shortcomings of our study. Because it was retrospective, many variables were uncontrolled, such as the lack of a standardized approach to evaluating anemia at birth. However, we did have a standardized neonatal blood transfusion guideline in place at all of our hospitals during the entire study period, to which we previously reported excellent adherence.[17,18] We also had standardized system-wide laboratory CBC analyzers.[19] In addition, there are certainly cases in which severe anemia at birth was recognized but did not require treatment and was not documented by the providers, and thus we recognize that our estimates of providers recognizing severe anemia at birth may be slightly lower than the actual number. Another limitation is the lack of routine Kleihauer–Betke or flow cytometry testing for fetal red blood cells in maternal blood samples of our neonatal patients with severe anemia of unknown cause. We speculate that fetomaternal hemorrhage has been underreported in our health care system because of the lack of studies of this condition.[9,20,21] Consequently, in cooperation with our Obstetric and Neonatal Operations at Intermountain Healthcare, we are developing a standardized approach to diagnosing fetomaternal hemorrhage. Another shortcoming is the racial makeup of our population, which is not representative of the US population. The extent to which this limits the generalizability of our findings is unclear. In addition, obstetric and neonatal care practices can affect the hemoglobin/hematocrit values at birth. These include delayed clamping of the umbilical cord,[22] umbilical cord milking,[23] and using fetal blood drawn from the umbilical cord after birth for the initial laboratory testing, thereby requiring less phlebotomy from the neonate.[24] These anemia-sparing practices were rarely used at the beginning of our study period (2011) and were introduced at our various delivery hospitals over the subsequent decade. Unfortunately, these elements are not possible to reliably evaluate by chart review. Thus, inconsistencies in these practices in our data diminish the generalizability of our results.

Two strengths of this study should be emphasized. First, the medical records of each of the 355 neonates were reviewed, because we did not want to rely on coded data. By reviewing each patient, we increased our confidence in determining whether the care team recognized anemia during the first day. Second, by constructing an algorithm to guide uniformity in selecting the most likely cause of anemia (**Figure 2**) before beginning the study, we believe that we improved uniformity of diagnosis.

From our present results, we conclude that using hemoglobin/hematocrit values below the 1st percentile is a feasible means of identifying severe anemia at birth, and that multiple causes of anemia—particularly the combination of hemorrhagic and hemolytic anemia—are more common in this group than previously appreciated. The association between hemorrhagic anemia and DIC is known. Severe acute hemorrhage can result in hypotension and critical acidosis that induces DIC with schistocytic hemolysis, further contributing to the severity of the anemia.

We speculate that implementing our 1st percentile anemia nomogram (**Figure 1**) in the EMR in each of our NICUs should promptly alert clinicians to the need for timely evaluation, and that implementing improved communication pathways with our obstetric colleagues regarding suspected fetomaternal hemorrhage will allow for Kleihauer–Betke and flow cytometry testing in more mothers whose infants have unexplained anemia at birth.

We look forward to system-wide implementation of our 1st percentile nomogram at all Intermountain Healthcare hospitals via the EMR, and we invite other interested NICUs to implement this tool as well. We have begun partnering with our clinical laboratories to use the nomogram to identify "critical values" of hemoglobin and hematocrit values at birth and to verbally report severely abnormal results from the laboratory technician to the responsible clinicians. We also have begun discussions with our obstetrics and transfusion medicine colleagues in an attempt to identify new ways to improve the detection, management, and outcomes of neonates who are severely anemic at birth. ■

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Reprint requests: Timothy M. Bahr, MD, Obstetric and Neonatal Operations, Department of Neonatology, Intermountain Healthcare, 5026 State St, Murray, UT 84107. E-mail: tim.bahr@imail.org

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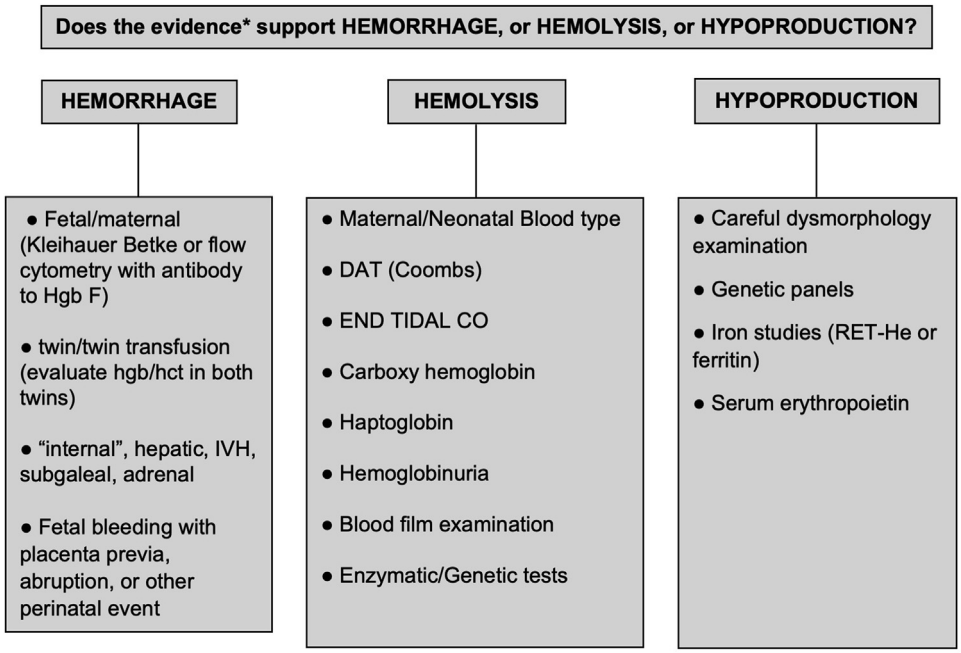

Figure 2. Methodology used for selecting the probable cause of anemia at birth. *The "first-line" evidence pertinent to the cause of neonatal anemia includes history (prenatal/birth and subsequent), physical examination, and CBC findings (reticulocyte%, absolute reticulocyte count, immature reticulocyte fraction, mean corpuscular volume, red blood cell distribution width). Second-line evidence of the cause of anemia (below) generally should focus on 1 of these 3 possibilities, unless first-line evidence does not clearly suggest a category or suggests a mixed mechanism. In such cases, tests from more than 1 column below may be appropriate. Hgb, hemoglobin; IVH, intraventricular hemorrhage; DAT, direct antiglobulin test; RET-He, reticulocyte hemoglobin content.

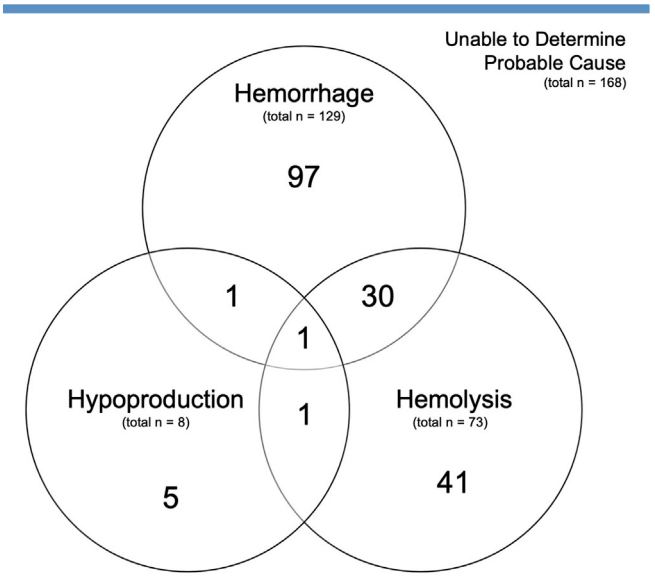

Figure 3. Venn diagram showing the probable causes of severe anemia at birth at Intermountain Healthcare in 2011-2020.

Table IV. Cases (N = 176) of severe anemia at birth in which a probable cause was listed in the medical record (N = 90) or was assigned retrospectively by the research team (N = 86) using the algorithm in Figure 2

Cases in which the probable cause of anemia at birth was identified (N = 176)	Cases where the cause was listed in the medical record (N = 90)	Cases where the cause was not listed in the record but was assigned by the research team (N = 86)	*P* value
Hemorrhage only	55	42	<.001
Hemolysis only	30	11	
Hypoproduction only	2	3	
Mixture of hemorrhage and hemolysis	3	27	
Mixture of hemorrhage, hemolysis, and hypoproduction*	0	1	
Mixture of hemorrhage and hypoproduction†	0	1	
Mixture of hemolysis and hypoproduction‡	0	1	

*Fetomaternal hemorrhage, DIC, and syndrome (46XX del 1q25.2-32.1).
†Fetomaternal hemorrhage and severe congenital iron deficiency.
‡DIC and congenital dyserythropoietic anemia type I.