

Anemia and Red Cell Distribution Width at the 12-Month Well-Baby Examination

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ABSTRACT

Background. Screens for anemia are among the most commonly done laboratory tests in children. The red cell distribution width (RDW) has been proposed as a diagnostic aid in the evaluation of pediatric anemias, but no prospective studies have been published describing its use.

Methods. A screening hematocrit determination done at the 12-month well-baby examination in 970 healthy infants yielded 62 low values (<33%), 31 of which were confirmed by heel stick complete blood count (CBC). After a 1-month trial of iron therapy, those with a rise in hemoglobin of at least 1 g/dL were considered to have iron-deficiency anemia. Nonresponders, after review of clinical and laboratory data (CBC, lead screen, and sickle screen), had hemoglobin electrophoresis if indicated.

Results. Abnormalities detected were iron deficiency, α -thalassemia, and hemoglobins SC and AS. These conditions were detected in 9 of 11 infants with abnormal RDW and none of 9 with normal RDW.

Conclusions. The RDW alone appears to be predictive of identifiable causes of anemia when used in screening 12-month-old babies who are otherwise healthy.

THE RED CELL DISTRIBUTION WIDTH (RDW) is an automated laboratory determination of red cell anisocytosis. It is the earliest laboratory predictor of iron-deficiency anemia.¹ The RDW with the mean corpuscular volume (MCV) is used to classify anemias in adults, but is seldom used in pediatric cases, perhaps because the differential diagnosis of pediatric anemias is not as broad as in older patients.²⁵ Use of the RDW alone to classify significant causes of anemia has not been previously published. We conducted an outpatient study at a hospital-based military clinic to prospectively test the ability of the RDW alone to predict iron deficiency and other causes of anemia in a general well pediatric population.

PATIENTS AND METHODS

All infants seen for the 12-month well-baby examination at the Pediatric Clinic, Womack Army Medical Center, Fort Bragg, North Carolina, over a 15-month period were included in the study. The standard screens were used (heel stick capillary tube spun hematocrit [HCT], lead screening, and sickle

preparation in black infants). Those with HCT values <33% had heel stick complete blood count (CBC) done with the Coulter Stack S electronic particle counter. All infants with a CBC HCT <33% received iron supplementation (3 mg/kg/day of elemental iron) for 1 month. Infants with abnormalities of other cell lines were excluded. Telephone follow-up was done at 2 weeks to assess compliance. At completion of the 1-month iron trial, a follow-up CBC was obtained. Infants with an increase of 1.0 g/dL or more in hemoglobin (Hb) concentration were considered to have iron deficiency and received an additional 2 months of iron therapy. Those with suboptimal response and persistent microcytosis or those with positive sickle preparation received hemoglobin electrophoresis. Iron studies were not done. The RDW was considered abnormal if >14.0, and the MCV was considered abnormally low if <72.5 fL.

RESULTS

Of the 970 infants who had screening HCT determination, 62 required further CBC evaluations. Of this group, 31 had a normal HCT value (at least 33%). Of the 31 who still had HCT values <33%, 20 completed the full protocol. Eleven patients were declared off protocol because of failure to obtain a 1-month fol-

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TABLE. Characteristics of 20 Anemic Patients

	Pre-Iron Values					Post-Iron Values					Hemoglobin Electrophoresis*	Diagnosis
	Hb	HCT	MCV	RDW	RBC	HB	HCT	MCV	RDW	RBC		
1	9.5	29.2	68.8†	14.1†	4.23	11.3	35.4	73.7	20.7	4.80		ID
2	9.1	30.0	59.2†	21.7†	5.07	11.1	35.6	69.7	30.7	5.11	Hb AA	ID/AT
3	10.1	29.9	76.6	14.8†	3.90	11.3	35.1	76.3	16.6	4.60		ID
4	7.8	25.3	57.8†	20.3†	4.38	10.9	35.5	65.1	31.8	5.44	Hb AA	ID/AT
5	10.0	30.0	75.5	14.8†	3.97	11.2	32.7	76.1	14.8	4.30		ID
6	9.4	28.3	70.7†	16.4†	3.99	12.0	36.1	74.9	18.5	4.82		ID
7	9.1	27.4	73.3	18.4†	3.79	9.2	28.3	70.8	17.6	3.96	Hb SC	SC
8	10.1	31.0	67.1†	14.4†	4.61	10.1	31.8	68.0	16.6	4.68	Hb AA	AT
9	10.5	31.2	72.0†	14.1†	4.32	11.1	34.4	71.9	14.6	4.72	Hb AS	AS/AT
10	8.8	25.3	79.8	12.2	3.17	9.6	29.2	89.5	24.8	3.26		Normal
11	10.9	32.9	72.8	13.1	4.52	11.3	34.6	74.0	13.6	4.67		Normal
12	11.1	32.6	74.0	13.6	4.41	10.0	30.2	73.7	13.8	4.09		Normal
13	10.5	31.1	82.3	11.9	3.77	11.0	33.1	82.3	11.8	4.02		Normal
14	9.9	30.2	82.7	12.8	3.64	10.8	32.4	84.0	13.8	3.85		Normal
15	11.3	32.3	79.2	13.6	4.07	11.7	35.7	78.8	12.1	4.52		Normal
16	10.8	31.6	83.9	11.8	3.77	11.3	32.7	83.9	11.8	3.77		Normal
17	10.1	31.0	75.1	13.5	4.13	10.6	32.2	72.6	14.3	4.43		Normal
18	10.5	30.3	85.8	12.9	3.52	10.7	32.3	85.5	12.8	3.78		Normal
19	10.3	31.0	77.0	16.6†	4.02	10.9	32.9	77.4	17.5	4.25		Normal
20	11.0	32.3	72.8	14.7†	4.43	10.3	31.2	74.7	15.0	4.17		Normal

*Done only if studies after iron therapy showed persistent microcytosis and anemia or if sickle prep was positive.

†Denotes abnormal MCV (< 72.5) or RDW (> 14.0) before iron therapy.

Hb = hemoglobin (g/dL), HCT = hematocrit (%), MCV = mean corpuscular volume (fL), RDW = red cell distribution width, RBC = red blood cell count (million/ μ L), ID = iron deficiency, AT = α -thalassemia, SC = SC disease, AS = sickle cell trait.

low-up CBC, administration of a non-standardized dose of iron by another provider, or because of military family relocation.

Nine of 11 infants with an abnormal RDW versus none of nine infants with a normal RDW had identifiable causes of anemia found ($P < .001$, two-sided Fisher's Exact Test). Thus an abnormal RDW had a sensitivity and specificity for known etiology of 100% and 81.8%, respectively. Combining both abnormal RDW with abnormal MCV increased the specificity to 100%, but decreased the sensitivity to 66.7%.

The abnormalities found were iron deficiency ($n = 4$), coexisting iron deficiency and α -thalassemia ($n = 2$), α -thalassemia ($n = 1$), coexisting α -thalassemia and hemoglobin AS ($n = 1$), and hemoglobin SC ($n = 1$). α -Thalassemia was presumed if there was persistent microcytosis (mean MCV 67.6 ± 1.7 fL after iron therapy), normal or increased red blood cell (RBC) count, and normal hemoglobin A_2 level. These patients had a mean HCT value of 29.1 ± 1.9 . After review of history and findings on physical examination, sickle preparations, and hemoglobin electrophoresis, the remaining 11 infants were considered to have normal states with a mean HCT of 31.5 ± 0.9 .

The 6 infants with iron-deficiency anemia had elevated RDWs (mean 17.1), and 4 of them also had low MCVs (mean, 68.1 fL). Of the 14 patients with non-iron-deficiency ane-

mia, 9 had normal RDW and MCV values, 3 had normal MCV and elevated RDW values (1 of these 3 had hemoglobin SC disease), and the final 2 had low MCV and elevated RDW values, presumably due to α -thalassemia; one of these also had hemoglobin AS. No abnormal results of lead screens occurred in any of the anemic patients.

DISCUSSION

It should be stressed that this study prospectively evaluated what is typically done in offices; that is, patients found to be anemic are given a diagnostic and therapeutic trial of iron supplementation. We simply looked for markers of iron-deficiency anemia in the screening laboratory test that most physicians order—the CBC.

Furthermore, even though some had known diagnoses, eg, Hb SC disease, all anemic infants were given a trial of iron therapy, which could unmask coexisting iron-deficiency anemia. Hemoglobin electrophoresis was not done in all nonresponders, since this is not typically done unless the CBC and smear are suggestive of thalassemia or the sickle preparation is positive.

Regarding iron deficiency, we have been evaluating infants in what we believe is a cost-effective manner, such as that proposed by Oski.⁶ All anemic infants are given a therapeutic trial of iron, and a hemoglobin increase of

at least 1 g/dL at one month is considered diagnostic of iron deficiency. We chose to monitor parameters that were highly associated with this disease state. An abnormal RDW is its earliest marker,¹ and the response to a therapeutic trial of iron is its most diagnostic finding.⁶ Iron studies to include iron binding capacity, ferritin, and free erythrocyte protoporphyrin measurements are impractical to obtain in a typical pediatric office setting at the time of the initial diagnosis of anemia. They certainly may be helpful later in the evaluation process as needed.

It is important to emphasize that our study identified iron-deficiency anemia only in those patients who were anemic (HCT <33%) and had a diagnostic increase in Hb after iron therapy. We did not include posttreatment change in HCT, MCV, RDW, or RBC as markers for iron-deficiency anemia. Review of our data would seem to indicate that if the rise in hemoglobin concentration of 1 g/dL was truly attributable to therapeutic iron, there would be a concomitant rise in HCT, MCV, RDW, and RBC. Patient 5 (Table) did not have an appreciable rise in these values, suggesting possible normal state rather than iron-deficiency anemia. Patient 10 did have an appreciable rise in HCT, MCV, and RDW suggestive of iron deficiency. This would have reduced the sensitivity and specificity of the abnormal RDW to 88.9% and 72.7%, respectively.

Anemia of mild inflammation may have been a factor in both iron-deficient and normal patients, though no acutely ill patients were included in the study. Children with recent acute infections tend to be anemic, and half may respond to diagnostic trials of iron, reiterating the link seen between anemia of chronic disease and iron deficiency.⁷

Our study appears to show that the RDW alone is a good marker of the normal versus abnormal state in an otherwise healthy infant who does not have any other cell lines affected and who has no evidence on history and examination of hemorrhage or chronic disease. Specifically, a normal RDW is highly predictive of a normal state. A much larger sample size is needed to validate these conclusions.

Finally, it should be noted that our patients are representative of the overall military population that has high follow-up medical care, which is available, free, and encouraged by the service member's unit. Routine dietary instruction and assistance are also readily available. In our institution, infants with significant illnesses, such as significant hemoglobinopathies or congenital heart disease, and premature infants born at less than 30 weeks' gestation are generally not followed up in the well-baby clinic. Furthermore, acutely ill infants are triaged out of the well-baby clinic. Thus our patient population and selection bias likely resulted in the low overall incidence of anemia (3.4%) and even lower incidence of iron-deficiency anemia (0.6%).

We agree with Oski's recommendation that the most prudent plan is to give a 1-month therapeutic and diagnostic trial to all anemic infants.⁶ Since a normal RDW appears predictive of non-iron-deficient states, repeated trials of iron therapy are not warranted. Furthermore, a normal RDW in an otherwise healthy infant is likely associated with a normal state. An abnormal RDW suggests a known etiology. We have found this useful in evaluating and treating children of all ages and would recommend it as a simple, cost-effective evaluation of anemia.

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