Reference Intervals in Neonatal Hematology

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KEYWORDS

• Complete blood count • CBC • Hemoglobin • Anemia • Erythrocyte indices
• Platelets • Leukocytes

KEY POINTS

- The various blood cell counts of neonates must be interpreted in accordance with high-quality reference intervals based on gestational and postnatal age.
- Using very large sample sizes, we generated neonatal reference intervals for each element of the complete blood count (CBC).
- Knowledge of whether a patient has CBC values that are too high (above the upper reference interval) or too low (below the lower reference interval) provides important insights into the specific disorder involved and in many instances suggests a treatment plan.

REFERENCE INTERVALS

In adult medicine, the elements of the complete blood count (CBC) can be recognized as normal or abnormal by comparing the patient's values with normal ranges established by drawing blood on large numbers of healthy adult volunteers. Normal ranges are not available for neonates, because of justified ethical concerns about drawing blood from healthy neonates for research purposes only. Consequently another approach is used, a concept termed reference intervals. These consist of 5th to 95th percentile values compiled from laboratory tests performed on selected neonates from whom a CBC was drawn for a clinical purpose. The process for selecting the data to be included in the reference range involves retrospectively identifying CBCs from

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neonates thought to have minimal disorders relevant to the laboratory test, or with disorders unlikely to significantly affect the test results.

To allow for reference ranges not being obtained on healthy volunteers, but on patients, the convention for the range used is different than for normal ranges. Normal ranges include 95% of the measured values, excluding the lowest and the highest 2.5%. In contrast, for reference ranges, 90% of values are included and the lowest and highest 5% are excluded, thus reference ranges are those between the 5th and the 95th percentile values.

Once the relevant database is set, the values within it are displayed in both of 2 ways: (1) data on the day of birth are shown according to gestational age, which is helpful when values at birth vary with gestational age, as is the case for many of the CBC parameters; (2) data on subsequent days are shown, thus illustrating the expected changes over the first weeks or months. These 2 data displays, focused on the 5th percentile value (lower range) and the 95th percentile (upper range) constitute reference intervals for neonates.

Over the past 7 years, we have published 15 reference interval studies focused on individual aspects of the CBC, all based on the Intermountain Healthcare datamarts.[1–15] Intermountain Healthcare is a not-for-profit company that owns and operates hospitals in Utah and Idaho. The present article brings together these individual reports into a single source. It is our hope that practitioners, rather than looking up the various individual publications, will consult this 1 source as a convenient and clinically useful resource.

METHODOLOGY

All reference intervals in this article were derived by identifying every CBC result performed on neonates in the Intermountain Healthcare system between 2005 and 2014. More than 350,000 individual test values were obtained on about 100,000 neonates. The number of values included in each reference interval varied by panel, ranging from a low of 3922 values for neutrophil counts of neonates of 22 to 28 weeks' gestation to a high of 216,869 values for platelet counts in the first 90 days of life. Patients who had an ICD9 (International Classification of Diseases, 9th Revision) code for a chromosomal abnormality were excluded. The neonate's record was matched to delivery information to ascertain the age of the baby in hours and days at the time of the test. Neonates who had received a red blood cell transfusion before their laboratory test for hematocrit, hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), or MCH concentration (MCHC) were excluded from the analysis. The average, 5th, and 95th percentiles were calculated (Statit, Corvallis, OR) and displayed by statistical trend lines.

INDIVIDUAL REFERENCE INTERVALS

Figs. 1–23 show the different neonatal CBC reference intervals. Each figure is constructed to show either the day of birth, giving reference intervals according to gestational age at birth, or postnatal age, giving reference intervals according to hours or days after birth. Where the CBC values for postnatal age vary significantly according to gestational age at birth, separate figures, based on gestational age, are provided. In each figure the 5th percentile is the lower reference interval and the 95th percentile is the upper reference interval. Both of these are shown by dotted lines. The average values are shown by solid lines.