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ARTICLE

Reference Ranges for Hematocrit and Blood Hemoglobin Concentration During the Neonatal Period: Data From a Multihospital Health Care System

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What's Known on This Subject

Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period have been published, but these used relatively small numbers of individuals and used methods that now are considered outdated.

What This Study Adds

We describe the effect of prenatal and postnatal age and gender on hematocrit and blood hemoglobin concentration. The figures aid clinicians who wish to know whether a hematocrit or hemoglobin determination falls within the reference range.

ABSTRACT

OBJECTIVE. "Reference ranges" are developed when it is impossible or inappropriate to establish "normal ranges" by drawing blood on healthy normal volunteers. Reference ranges for the hematocrit and the blood hemoglobin concentration of newborn infants have previously been reported from relatively small sample sizes by using measurement methods that now are considered outmoded.

METHODS. We sought to develop reference ranges for hematocrit and hemoglobin during the neonatal period (28 days) by using very large sample sizes and modern hematology analyzers, accounting for gestational and postnatal age and gender. Data were assembled from a multihospital health care system after exclusion of patients with a high likelihood of an abnormal value and those who were receiving blood transfusions.

RESULTS. During the interval from 22 to 40 weeks' gestation, the hematocrit and blood hemoglobin concentration increased approximately linearly. For every week advance in gestational age, the hematocrit increased by 0.64% and the hemoglobin concentration increased by 0.21 g/dL. No difference was seen on the basis of gender. During the 4-hour interval after birth, hematocrit/hemoglobin values of late preterm and term neonates (35–42 weeks' gestation) increased by 3.6% ± 0.5% (mean ± SD), those of neonates of 29 to 34 weeks' gestation remained unchanged, and those of <29 weeks' gestation decreased by 6.0% ± 0.3%. During the first 28 days after birth, an approximately linear decrease in hematocrit/hemoglobin occurred.

CONCLUSIONS. The figures presented herein describe reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period, accounting for gestational and postnatal age. *Pediatrics* 2009;123:e333–e337

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THE HEMATOCRIT AND the blood hemoglobin concentration are among the most commonly performed of all clinical laboratory tests.[1] Many publications have sought to establish reference ranges for hematocrit and hemoglobin concentration among neonates[2–11]; however, most such studies involved fewer than 100 patients and used methods less accurate than those used in modern hematology analyzers. For instance, the reference ranges in general use today are taken from hematocrit values obtained after spinning a blood sample in a microcentrifuge.[12,13] That method introduced variability as a result of technician inconsistencies, differences in the amount of trapped plasma, and variable erythrocyte size.[13] Modern hematology analyzers electronically measure the erythrocyte volume and multiply this by the erythrocyte concentration, also measured electronically.[14] The hematocrit and the blood hemoglobin concentration, which is determined spectrophotometrically, are now generally performed by using a single instrument that uses logs higher sample sizes than the original methods.[14] Little has been published, using any method, on the reference ranges of hematocrit and hemoglobin among extremely low birth weight neonates (<1000 g). For these reasons, we sought to describe the reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period of neonates 22 to 42 weeks' gestation by using modern instrumentation and large sample sizes.

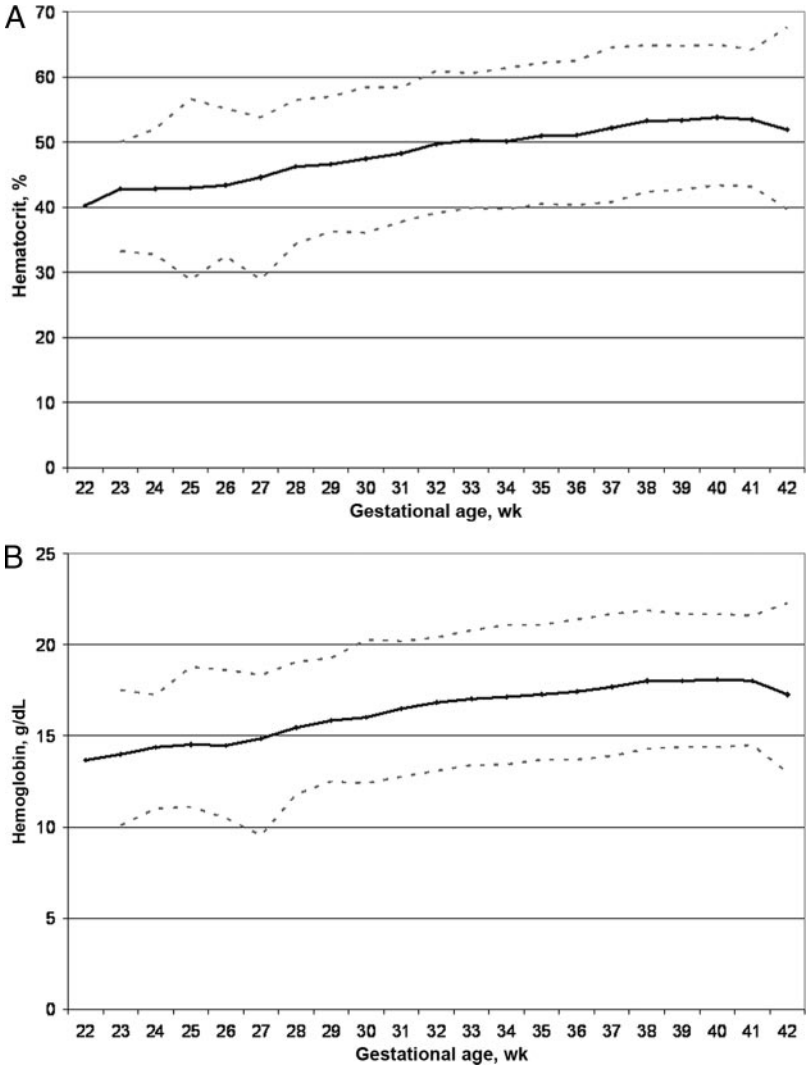

FIGURE 1
The reference ranges are shown for hematocrit (A) ($N = 25\,464$ patients) and blood hemoglobin concentration (B) ($N = 24\,416$ patients) at 22 to 42 weeks' gestation. Tests were obtained during a 6.5-year period (January 2002 through June 2008). Values were excluded when the diagnosis included abruption, placenta previa, or known cases of fetal anemia or when a blood transfusion was given before the first hematocrit was measured. The solid line shows the mean value, and the dashed lines show the 5% and 95% reference range.

METHODS

Information was collected as a deidentified limited data set from archived electronic Intermountain Healthcare records. The information collected was limited to that displayed in the figures of this report. Laboratory values were analyzed from patients with a date of birth from January 1, 2002, through June 30, 2008. The tests analyzed were those run on a Beckman Coulter Hematology Analyzer (Fullerton, CA),[14] which were obtained for clinical use from patients who had not received an erythrocyte transfusion and were not excluded because of associated conditions. Specifically, data were not included when the patient had a diagnosis of neonatal anemia or when the mother had the diagnosis of placenta previa or abruptio placenta. Gestational age was determined by obstetric assignment unless this was changed by the neonatal examination.

The program used for data collection was a modified subsystem of "clinical workstation." Clinical workstation is a Web-based electronic medical chart application that stores demographic and clinical information, such as history, physical examination results, laboratory data, problem lists, and discharge summaries. 3M Co (Minneapolis, MN) approved the structure and definitions of all data points for use within the program. The data were collected from the electronic medical chart, laboratory systems, and case mix. Case mix is the billing, coding, and financial data mart used by Intermountain Healthcare.

Data were managed and accessed by authorized data analysts. Descriptive statistics were calculated using Statit (Corvallis, OR). Mean values and 5th and 95th percentiles were used to express the data. The 5th and 95th percentiles were calculated by looking at all of the points and selecting a value at which 5% of the total values were greater or less than that value. Mean values were statistically analyzed using a Student's t test. Statistical significance was set as $P < .05$. The Intermountain Healthcare institutional review board approved the study.

RESULTS

Reference ranges for hematocrit and blood hemoglobin concentration over the interval of 22 to 42 weeks' gestation are shown in Fig 1. Hematocrit values were in-

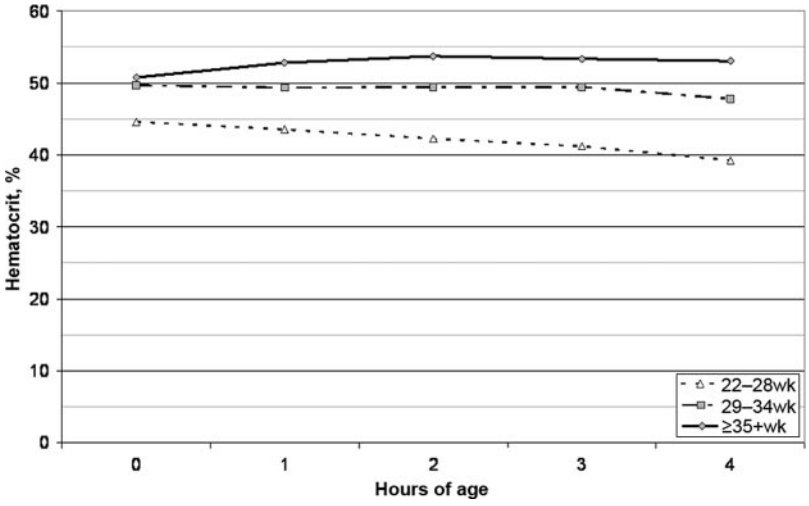

FIGURE 2
Mean values are shown for hematocrit ($N = 23\,534$) at delivery and during the first 4 hours after birth. Three groups of neonates are shown, according to gestational age (35–42 weeks, 29–34 weeks, and 22–28 weeks).

cluded from 25 464 patients and hemoglobin values from 24 416. All were obtained within 6 hours of birth. An approximately linear increase in hematocrit/hemoglobin is observed between 22 and 40 weeks. Multiple linear regression indicated that for every week advance in gestational age (GA), the hematocrit increased according to the formula [hematocrit = 28.59 + (GA × 0.6359)], and the hemoglobin concentration increased according to the formula [hemoglobin = 9.92 + (GA × 0.2087)]. No effect of gender was found on hematocrit or hemoglobin.

The hematocrit of 32 534 patients and the blood hemoglobin concentration of 22 621 patients during the first 4 hours after birth are shown in Fig 2. Hematocrit and hemoglobin increased during the first 4 hours after delivery among late preterm and term neonates (gestational age 35–42 weeks) with a hematocrit increase of 3.6% ± 0.5% (mean ± SD; $P < .001$). No change in hematocrit/hemoglobin was observed during this period among the group of neonates 29 to 34 weeks' gestation, and a fall was seen in the group <29 weeks' (decrease in hematocrit of 6.0% ± 0.3%; $P < .001$; Fig 2).

Reference ranges for hematocrit ($n = 41\,957$) and blood hemoglobin concentration ($n = 39\,559$) during the neonatal period (first 28 days) are shown in Fig 3. All values from patients who received ≥1 erythrocyte transfusion in the first 28 days were excluded from the reference ranges. Patients had an approximately linear fall in hematocrit/hemoglobin between the day of birth and day 28. Those born at 35 to 42 weeks' gestation (Fig 3A) began with a mean hemoglobin value of 18 g/dL (5% value; 14 g/dL), which fell to 13 g/dL (5%; 9.5 g/dL) at 28 days. Patients who were of 29 to 34 weeks' gestation began with lower hematocrit/hemoglobin values that fell further (to 11 g/dL; 5%; 7.8 g/dL) by 28 days. So few patients who were of <29 weeks' gestation had no erythrocyte transfusions that reference ranges for the first 28 days could not be calculated reliably on that group.

DISCUSSION

"Normal ranges" are not available for hematocrit and hemoglobin of neonates because blood is not drawn on healthy, normal neonates to establish such ranges. Instead, "reference ranges" are used. These consist of the 5th to the 95th percentile values compiled from tests that are performed on neonatal patients who are thought to have minimal pathology relevant to the test or pathology unlikely to affect significantly the result of the test. The premise on which a reference ranges is based is that these values approximate normal values, although they were obtained for a clinical indication, not from healthy volunteers.

In this study, we sought to establish reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period (first 28 days) by using large sample sizes and standardized hematology analyzers. We first sought to assess the effect of gestational age and thus collected values obtained in the first hours after birth from neonates of 22 to 42 weeks' gestation. In keeping with the reference range concept, we sought to exclude data from patients with a high likelihood of an abnormal value or who had received a blood transfusion. By retrieving >20 000 values from the Intermountain Healthcare data marts, we observed that the hematocrit and blood hemoglobin concentration increase gradually and approximately linearly between 22 and 40 weeks' gestation. This gradual increase during gestation was not clear from previous reports.[15–17] The effect of gender on the initial hematocrit/hemoglobin was also previously unclear,[2–13] but by using this large data set, we now confidently conclude that there is no relationship.

The reference range that we observed for hematocrit at birth among term neonates is 42% to 65%. This range is similar to the values in general use in neonatology.[13] Changes in hematocrit/hemoglobin during the 4-hour period after delivery were described by Gairdner et al,[18] who reported an increase of ~5% during this period. He ascribed this increase, at least in part, to intravascular concentration of blood received by placental transfusion.

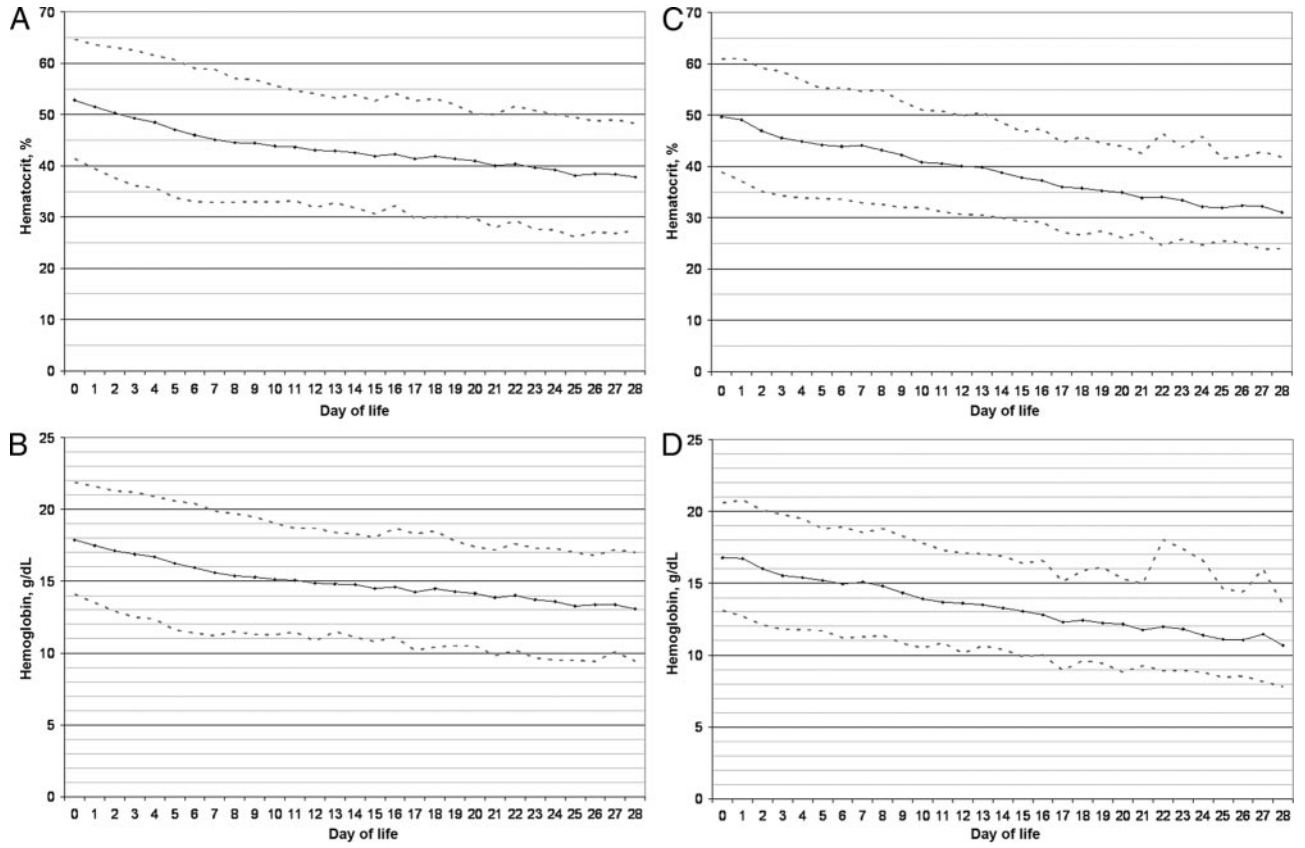

FIGURE 3

The reference ranges are shown for hematocrit (A and C) ($N = 41\,957$ patients) and blood hemoglobin (B and D) ($N = 39\,559$ patients) during the 28 days after birth. Values were divided into 2 groups (A/B and C/D) on the basis of gestational age at delivery. Patients were excluded when their diagnosis included abruption, placenta previa, or fetal anemia or when a blood transfusion was given. Analysis was not possible for patients <29 weeks' gestation because virtually all of these had repeated phlebotomy and erythrocyte transfusions. A and B, Late preterm and term infants (35–42 weeks' gestation); C and D, preterm infants (29–34 weeks' gestation).

Whether this postbirth increase also occurs in preterm infants has not previously been known. We found no postbirth increase among the group of neonates who were of <35 weeks' gestation. Moreover, we found a fall in hematocrit/hemoglobin during this early interval among the group who were of <29 weeks' gestation. We speculate that the lack of a postbirth increase among preterm infants owes to the lack of a significant placental transfusion, from the practice of rapidly clamping the umbilical cord to pass the neonate immediately to the neonatologist. We are uncertain about the explanation for the postbirth fall among the group <29 weeks. One possible explanation is early net fluid shifts with extravascular fluid moving into the vascular space, resulting in a dilutional fall in hematocrit/hemoglobin. Early administration of intravenous fluids to those <29 weeks might be a contributing factor. Early phlebotomy losses might also be involved, including losses obtained for initial laboratory studies, blood cultures, and blood bank testing. Subsequent movement of fluid into the intravascular space to compensate for the phlebotomy losses could be a factor.

Physiologic changes in hematocrit and hemoglobin concentration during the neonatal period are difficult to interpret among the smallest patients because of the confounding issues of periodic phlebotomy losses and blood transfusions. A clearer picture of physiology is seen among the relatively healthy late preterm and term neonates who have few phlebotomy losses and no transfusions. Figure 3 shows the hematocrit/hemoglobin during the first 28 days in such patients. The values fall, approximately linearly, during the first 28 days after birth. Preterm infants generally begin with a slightly lower hematocrit/hemoglobin level, which falls more rapidly and to a lower value on day 28, than among term infants.

We recognize various limitations and pitfalls to our present study, which should be considered when applying these findings to practice. First, the neonates whose blood data were used for these studies were at altitudes ranging from ~2600 to 5000 ft above sea level (800–1520 m). Studies at similar altitudes in Colorado indicate that pregnant women have a hematocrit ~2.5% higher than at sea level; however, umbilical cord blood of deliveries at 5000 to 5500 ft does not differ from cord blood at sea level in arterial or venous O_2 content, O_2 saturation, or hemoglobin concentration.[19] At very high altitudes (14 000–18 000 ft [4370–5500 m]), maternal hematocrit levels are significantly higher than at sea level,[20,21] and fetal hematocrit levels are minimally

higher than at sea level.[22] On the basis of these comparisons, we assume that the reference ranges that we report in this study are similar to those expected at sea level.

A second limitation is that the exact source of the blood samples tested (capillary, venous, arterial) was not recorded. The figures in this article are therefore from a mixture of sources. Hematocrit values obtained from capillary beds of neonates tend to be higher than those simultaneously obtained from vascular sources.[13] Oh and Lind[23] suggested this is attributable, at least in part, to the larger size of erythrocytes in neonates, which may flow more slowly through capillary beds and lead to hemoconcentration of capillary blood. Another study limitation is that, although we attempted to exclude data from patients with anemia and those who received a blood transfusion, it might be that some patients with pathologic anemia were inadvertently included. Had we tested only entirely healthy neonates, the 5th to 95th reference ranges would likely be somewhat narrower than shown in the figures.

Hematocrit and blood hemoglobin concentration are measured frequently in ill neonates. We maintain that the figures presented here can assist clinicians who seek to determine whether values obtained on their neonatal patients fall within or outside the reference ranges.

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