Red Cell Distribution Width (RDW) in the Newborn: Normative Data

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Aim: To evaluate the normal range of red blood cell distribution width (RDW) in term and preterm newborns dependent on gestational age. **Material and methods:** A total of 1,594 preterm and term neonates were admitted to our neonatology department. Infants were divided into two groups according to their gestational age. Group 1 consisted of infants with ≤ 34 weeks of gestation; group 2 consisted of infants with ≥ 35 weeks of gestation. Infants in Groups I and II were subdivided according to their gestational age. Gestational age, birth weight, sex, hemoglobin and hematocrit, MCV levels of all newborns were recorded, and RDW was compared between the groups. **Results:** A total of 1,594 newborns

were enrolled in the study. Group 1 (≤ 34 weeks) consisted of 725 newborns and Group 2 (≥ 35 weeks) consisted of 869 newborns. The mean normal range of RDW in Group 1 was 17.8 ± 2.1 and of group II was 16.7 ± 1.6 ($P < 0.05$). The normal range for RDW values at 32–34 weeks was higher than at 35–36 gestational weeks, and at 37–42 weeks ($P = 0.002$ and 0.003). **Conclusion:** RDW values at ≤ 34 weeks in newborns are higher than at ≥ 35 weeks. This may be useful in the differential diagnosis of neonatal hematologic diseases together with other red cell parameters. J. Clin. Lab. Anal. 25:422–425, 2011. © 2011 Wiley Periodicals, Inc.

Key words: red cell distribution width; RDW; newborn; gestational age; normative; data

INTRODUCTION

Red blood cell distribution width (RDW) is a quantitative measure of variability in the size of circulating erythrocytes, and is a statistical value that is obtained from erythrocyte histograms. It shows a distribution width according to size (1,2). RDW is routinely reported to physicians in clinical practice as part of the automated complete blood count (CBC) and is mainly used as an auxiliary index in the differential diagnosis of anemia (1,2). The diameter of the red blood cell was first measured by Jurlin in 1718. Afterwards, the first quantitative assessment of variation in red blood cell diameter was reported by Prince-Jones (in 1910, 1922, and 1933, respectively) using ocular micrometry on fixed stained peripheral blood smears from normal individuals and from patients with a variety of anemia (3). Through developments in technology, the change from chamber counts to flow-cytometry for routine blood counts in some recently designed automated cell counters has brought not only improved speed and

precision but also new measurements permitted by analysis of large numbers of single cell measurements (3). Nowadays, most electronic counters calculate the co-efficient of variation in red cell volume and report as RDW, the heterogeneity of the distribution of red cell size.

The normal hematologic values in neonates differ significantly from those in older children and adults (4). Normative data for RDW values in both term and preterm infants are limited and inconsistent, and these values have been used according to adult values in most of the routine blood counters. Furthermore, no enough normative data are available on the normal value for

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RDW in newborn infants both term and preterm according to gestational age (4). In this study, we have aimed to determine normal ranges in RDW value for newborns within the early days of life.

Patients and Methods

During a 4-year period (from September 2005 to September 2009), we prospectively evaluated all 1,594 consecutive preterm and term neonates admitted to our neonatology department, all of which were apparently clinically and hematologically normal. Ethical approval was obtained from hospital ethical committee and informed consent was obtained from the parents, before the blood was drawn. A detailed history of both newborns and families were taken, and clinical examination was performed. Newborns with any medical conditions such as infection, hospitalization, hydrops fetalis, intrauterine transfusions, twin-to-twin transfusion, low APGAR score (<5), grade 3 or 4 intraventricular hemorrhage detected by the third postpartum day, small for gestational age (birth weight, 10th percentile for gestational age), discordant twins (difference in birth weights between the twins that is 20% of the weight of the larger twin), fetomaternal hemorrhage, severe chromosomal anomalies, cyanotic congenital heart disease, any shock-like state in the immediate postpartum period, disseminated intravascular coagulation, and positive antibody titers other than those attributable to RhoGAM, and maternal medications that may affect the fetal hemopoietic system, emergency cesarian section secondary to significant antenatal bleeding, intravenous fluid boluses given before obtaining the blood sample, chronic hypoxia or positive family history in terms of hematologic diseases such as thalasemias were excluded.

Blood samples were taken from all newborns on the first day of life. Two milliliters of blood was collected from a peripheral vein into a K_3 EDTA tube (tripotassium ethylenediamine tetraacetic acid) and counts were performed within 1 hr of sample collection, since a decrease in RDW with prolonged storage of the specimen at room temperature may occur (3,5). Hematological parameters were determined with a Sysmex-XT-2000i counter (Sysmex, Kobe, Japan). The patients were divided into two groups according to their gestational age. Group 1 consisted of patients at ≤ 34 weeks of gestational age, and group 2 consisted of patients at ≥ 35 weeks of gestation. In addition, the patients in both groups were subdivided according to gestational age. Gestational age, birth weight, sex, hemoglobin (Hgb), and hematocrit (Hct) parameters of all newborns were recorded, and RDW was compared between the two groups.

Statistical Analysis

All statistical analyses were performed using the SPSS program, version 15.0 (Chicago, IL). Normal distribution of variables was tested with Shapiro–Wilk test, and normal distribution of data was determined. Next, data were compared between the two groups with *student t* test. One-way ANOVA with Bonferoni was used for intergroup analyses for subgroups. Parameters were given as mean $\pm$ standard deviation (SD). *P* values of less than 0.05 were considered statistically significant.

RESULTS

During the study period, 1,594 newborns were enrolled in the study. Group 1 (≤ 34 weeks of gestational age) consisted of 725 newborns and Group 2 (≥ 35 weeks of gestational age) consisted of 869 newborns. Seven hundred and nineteen patients (45.1%) of all newborns were girls and the remaining of 875 patients (54.9%) were boys. Mean birth weight, Hgb, and Hct of all patients were $2,954 \pm 699$ g, 17.4 ± 2.6 g/dl, and $52.2 \pm 6.9\%$, respectively. There were no significant differences between Groups 1 and 2 in terms of gender, Hgb, and Hct levels, except birth weight ($P < 0.05$). Mean normal range of RDW in Group 1 was 17.8 ± 2.1 and of group II was 16.7 ± 1.6 ($P > 0.05$). Significant difference was found in terms of gender between Groups 1 and 2. Two groups were divided into subgroups. Table 1 shows descriptive data of both groups and subgroups. Newborns in Group 1, 168 newborns were < 30 weeks of gestational age, 246 newborns were 30–31 weeks of gestational age, and 311 newborns were 32–34 weeks of gestational age. However, newborns in Group 2, 393 newborns were 35–36 weeks of gestational age, and 476 newborns were 37–42 weeks of gestational age. Mean normal ranges of RDW in the other subgroups are shown in Table 2. Mean normal range for RDW values in newborns at < 30 weeks of gestation was higher than those in newborns at 31–32 weeks of gestation, 35–36 weeks of gestation, and 37–42 weeks of gestation ($P = 0.036$, $P = 0.004$, and $P = 0.002$, respectively). However, there were no significant differences between mean normal range for RDW values in newborns at < 30 weeks of gestation and 32–34 weeks of gestation ($P = 0.65$). Additionally, no significant differences were found among the mean normal range for RDW in newborns at 31–32 weeks, 35–36 weeks, and 37–42 weeks of gestation ($P > 0.05$). Mean normal range for RDW values in newborns at 32–34 weeks of gestation was higher than in newborns at 35–36 weeks of gestation and at 37–42 weeks of gestation ($P = 0.002$, and $P = 0.003$, respectively). Finally, there were no significant differences among all subgroups in terms of gender.

TABLE 1. Descriptive Data of Group 1 and Group 2

Variables	Group 1 (n = 725) (mean $\pm$ SD)			Group 2 (n = 869) (mean $\pm$ SD)		P
	<30 weeks (n = 168)	31–32 weeks (n = 246)	32–34 weeks (n = 311)	35–36 weeks (n = 393)	37–42 weeks (n = 476)	
Gender (female/male)	81/87	111/135	151/160	163/230	213/263	> 0.05
Birth weight (g)	1,185 $\pm$ 289	1,576 $\pm$ 277	2,021 $\pm$ 468	2,598 $\pm$ 438	3,264 $\pm$ 458	< 0.05 ^a
Hemoglobin (g/dl)	16.52 $\pm$ 2.7	17.22 $\pm$ 2.2	17.54 $\pm$ 2.1	17.45 $\pm$ 2.13	17.3 $\pm$ 1.98	< 0.05 ^b
Hematocrit (%)	49.7 $\pm$ 8.9	51.5 $\pm$ 7.8	54.5 $\pm$ 7.4	54.3 $\pm$ 7.2	53.2 $\pm$ 6.9	< 0.05 ^b
MCV (fl)	115.6 $\pm$ 5.4	114.0 $\pm$ 7.3	113.4 $\pm$ 6.2	117 $\pm$ 5.4	119 $\pm$ 9.3	< 0.05 ^c

MCV, mean corpuscular volume.

^aSignificant differences among all groups.

^bSignificant differences between <30 week of gestation and the other groups.

^cSignificant differences between 35–36 weeks and 37–42 weeks and the other groups.

TABLE 2. Normal Range of RDW According to Subgroups

Variable	Group 1 (n = 725)			Group 2 (n = 869)	
	^a <30 weeks (n = 168)	^b 31–32 weeks (n = 246)	^c 32–34 weeks (n = 311)	35–36 weeks (n = 393)	37–42 weeks (n = 476)
RDW (mean $\pm$ SD)	17.67 $\pm$ 2.283	16.9 $\pm$ 1.98	17.86 $\pm$ 2.23	16.81 $\pm$ 1.82	16.65 $\pm$ 1.81

RDW, red blood cell distribution width.

^aSignificant differences between <30 weeks of gestational age newborns and other groups, except 32–34 of gestation.

^bSignificant differences between 31–32 weeks of gestation and other groups, except 35–36 and 37–42 weeks of gestation.

^cSignificant differences between 32–34 weeks of gestation and other groups, except <30 weeks of gestation.

DISCUSSION

In this study, we aimed to determine normal values of RDW in subgroups of preterm and full-term neonates according to different gestational ages. These data enabled us to determine whether RDW is dependent on gestational age. To our knowledge, there are no previously reported definite RDW values comparing gestational age in newborns. Therefore, the results of this study would be useful to define the normal values of RDW in groups according to gestational age for the diagnosis of neonatal hematologic diseases along with other red blood cell parameters.

RDW is typically elevated in conditions of ineffective red cell production, such as iron deficiency, B12 or folate deficiency, or hemoglobinopathies, increased red cell destruction such as hemolysis or after blood transfusion in children and adults. At the beginning, RDW has been used for the differential diagnosis of certain anemias, and reported to be a good index to differentiate between iron deficiency anemia (IDA) and thalassemia minor (6–8). Although there is still some controversy regarding its reliability. During recent years, some studies have reported that RDW alone is not sufficiently specific or sensitive enough to differentiate between microcytic

anemias. Furthermore, it may be misleading for the diagnosis of anemias, as all thalassemia cases had an equally elevated level of RDW compared with IDA, and elevated values were not specific for IDA (9–12). This may be explained by the fact that an elevated RDW may be caused by several factors such as erythrocytosis, the presence of target cells, and elevated reticulocyte counts (5,13). Additionally, some studies have recently evaluated the clinical relevance of RDW on adult diseases, particularly on heart diseases. However, some contradictory results have been found on this issue. Some studies have supported that RDW is a good prognostic marker for cardiovascular diseases, but some have not supported such a finding (14,15). On the other hand, there is no known clinical relevance of RDW on the diseases of newborns. The results of this study may help for such studies on the diseases of newborns.

In newborns, the normal values of RDW have been previously found higher than those of other children groups, but the normal values in more subdivided age groups in preterm infants are lacking with few reports (4,16). Kook et al. (3) has reported previously that the normal range of RDW in newborns is 17.1 $\pm$ 1.7, independent from gestational age. However, Alur et al. (17) have evaluated red blood cell indices in very

low-birthweight infants involving RDW and concluded that RDW values are affected by gestational age in addition to Hct and Hgb values. In this study, our results indicated that RDW values are different among gestational ages and gestational age affects the RDW values. The speculation that the observed increase in RDW might be due to increased erythropoiesis dependent on the gestational age. The fact is that erythropoiesis depends on gestational age, and increases 3–5 fold in the last trimester. Additionally, most of the elevated RDW levels in preterm infants involve at 32–34 weeks of gestational age (6). Therefore, the results of this study indicate that the normal range for RDW values at 32–34 weeks is higher than those at 35–36 gestational weeks and at 37–42 weeks of gestational age.

In conclusion, during the newborn period, the normal range of RDW differs among newborns in terms of gestational age, and RDW values is not different among the groups according to gender. Additionally, our results suggest that RDW values should be evaluated according to these specific results for diagnosis of newborn blood disease without respect to adult or child values. Because, RDW in neonates is elevated as compared with that in adults and reflects significant variability in the size of the RBCs (6). If these are taken into consideration, our study could be useful as a baseline of RDW values in newborns. Further studies are needed on this issue.

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