Reference Range of Complete Blood Count in Healthy Term Newborns 1 Week after Birth

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Abstract

BACKGROUND: Determination of the complete blood count (CBC) and reticulocyte reference range helps diagnose a disease related to changes in erythrocyte indices, white blood count, platelets, and reticulocytes, especially in newborns.

AIM: The aim study is to establish a reference range for CBC and reticulocyte in healthy term newborns 1 week after birth.

MATERIAL AND METHODS: The study method is prospective analyses of CBC and reticulocyte in term newborns within 1 week after birth. Inclusion criteria are term newborn (gestational age 37–42 weeks) with good tone, breathing, or crying immediately, do not have resuscitation, and the birth weight is ≥2500 g.

RESULTS: Two hundred and seventy-seven term newborns met the inclusion criteria. There were 145 (52.35%) male infants and 132 (47.65%) female infants. The reference range of newborns for hemoglobin (Hb) at P2.5–P97.5, P3–P97, P5–P95, and mean ± 2 standard deviation (SD) was 11.70–19.60 g/dL, 11.90–19.57 g/dL, 12.20–19.20 g/dL, and 11.35–19.63 g/dL, respectively. In addition, reference range of male newborns for Hb at P2.5–P97.5, P3–P97, P5–P95, and mean ± 2SD was 12.20–20.14 g/dL, 12.28–19.91 g/dL, 12.63–19.38 g/dL, and 11.47–20.15 g/dL, respectively. The reference range of female newborns for Hb at P2.5–P97.5, P3–P97, P5–P95, and mean ± 2 SD was 11.37–19.20 g/dL, 11.50–19.20 g/dL, 11.80–19.20 g/dL, and 11.37–18.93 g/dL, respectively.

CONCLUSION: The reference range of CBC and reticulocyte for healthy term newborns, male newborns, and female newborns in this study can be used as a benchmark.

Introduction

The reference range of the complete blood count (CBC) and reticulocyte in the newborn is limited, especially in Indonesia. Meanwhile, determining the reference range of the CBC and reticulocyte value is very important to help doctors when a newborn baby looks pale, has bleeding, or has a neonatal infection in subsequent care. That is why determining the reference range of the CBC and reticulocyte in the newborn is crucial.

All ages' anemia prevalence was 22.8% globally in 2019. The prevalence was highest among children under 5 years, 39.7%, with the most contributing cause, was dietary iron deficiency (ID) [1]. Anemia defined as a low hemoglobin (Hb) concentration according to age. Anemia is still a global public health problem, so early detection is crucial to prevent it. Aziz *et al.*'s study found that the prevalence of ID anemia (IDA) at birth was 22.8% from 368 term newborns [2]. Meanwhile, another study of 211 newborns found that the incidence of iron depletion, ID, and IDA was 9.5%, 14.2%, and 11.85%, respectively [3].

Low iron stores at birth, eminent postnatal growth velocity, and iron loss cause ID [4], [5], [6].

Iron plays a key role in developing the central nervous system and is essential to neural myelination and neurotransmitter function [7], [8]. Therefore, starting early enteral iron supplementation in term newborns is proposed to avert ID [3]. If oral iron supplementation is late to an infant, neurological disorders will manifest in the long term [9]. Although ID can be corrected by iron supplementation, the cognitive and behavioral deteriorations observed in children with ID may not be completely restorable [10], [11]. Thus, some term infants still develop ID even with iron supplementation so that early ID detection would be ideal.

The purposefulness of the lower limit of Hb concentration to declare someone anemic or not depends on the person's age, type of race, gender, and demographics area in which the person lives. On the other hand, other erythrocyte indices reference range is needed to establish the diagnosis of anemia. Moreover, determining the CBC and reticulocyte reference range helps diagnose a disease related to erythrocyte indices, white blood count, platelets, and reticulocytes. Therefore, the study aims to establish reference range of CBC and reticulocyte in healthy term newborns 1 week after birth.

Material and Methods

Study population

This prospective analysis was carried out at a secondary hospital evaluating laboratory data obtained as a routine admission procedure. The research sample was a newborn baby delivered from April 2018 to December 2018 (9 months period) at Idaman Banjarbaru Hospital. Inclusion criteria are term newborn (gestational age 37–42 weeks) with good tone, breathing, or crying immediately, do not have resuscitation, and the birth weight is ≥2500 g [12]. Exclusion criteria were hematological diseases, congenital anomalies, or the lack of a CBC within 1 week after birth. In addition, gestational age, birth weight and length, and head and chest circumference were obtained from the newborn's medical record. All of the newborn's parents had signed the informed consent. This study had obtained ethical clearance from the Research Ethics Commission of Medical Faculty of the University of Lambung Mangkurat No. 535/KEPK-FK ULM/EC/II/2021.

Blood sampling

Every newborn who meets the inclusion and exclusion criteria will be taken a blood sample of 1 ml from the median cubital vein. The blood sample was put in a tube with EDTA anticoagulant, homogenized by turning it over, and stored in a storage box. Then, the blood sample was sent to the Banjarbaru Idaman Hospital Laboratory. CBC examinations were carried out by inserting a sample of the baby's blood into the Sysmex XN-450 Hematology Analyzer.

Statistical analysis

All newborn anthropometry measurements and laboratory findings of CBC and reticulocyte are analyzed by SPSS ver.25 for P2.5, P3, P5, P95, P97, P97.5, and mean and standard deviation (SD). All data are presented

Discussion

Ferritin, soluble transferrin receptor (sTfR), and transferrin saturation are the best parameters to assess a person's iron status, including newborns. One study, using indicators of CBC, ferritin, sTfR, and transferrin saturation, found that the incidence of iron depletion, ID, and IDA was highest in infants aged 0 months, 9.5%, 14.2%, and 11.8%, respectively [3]. The problem is that the examination requires substantial blood, is influenced by the diurnal phase, inflammation, infection, is expensive, and is limited to specific health facilities. This research is intended to find alternative tests that can determine the iron status of newborns 1 week after birth and to evaluate the severity of the ID so can make early prompt treatment of ID. The CBC examination can be performed in conjunction with the peripheral blood smear examination. The blood drawn is small, easy to do, cheap, not affected by inflammatory or infectious factors, and widely available in health facilities.

In 2008, a study in newborns showed a reference range of CBC values with P2.5–P97.5 [13]. However, in the past 13 years, there has been no updated data of the CBCs reference range for healthy term newborns. The in-charge doctor ensures the healthiness of newborns by physical examination with good tone, breathing, or crying immediately, does not have resuscitation weighing >2500 g. The lower limits of body length and head circumference of all infants in this study were above the WHO growth curve's 3rd percentile (P3); this further confirms that all infants were healthy and physically normal in size [14]. This study showed the reference range of CBC and reticulocyte at P2.5–P97.5, P3–P97, P5–P95, and mean ± 2SD. Thus, for example, this study indicates that the lower limit of Hb for healthy term newborns can be taken at P2.5, P3, P5, or mean-2SD, that is, 11.70 g/dL, 11.90 g/dL, 12.2 g/dL, or 11.35 g/dL, respectively. This study also showed that the P2.5, P3, P5, and mean-2SD values of Hb for male newborns were 12.20 g/dL, 12.28 g/dL, 12.63 g/dL, or

Table 1: The reference range of CBC and reticulocyte in healthy term newborns 1 week after birth

CBC	N	$P_{2.5}$–$P_{97.5}$	P_3–P_{97}	P_5–P_{95}	Mean ± 2SD
WBC (10³/uL)	277	8.04–30.37	8.37–30.11	9.23–26.14	6.83–28.31
RBC (10⁶/uL)	277	3.25–5.55	3.31–5.49	3.41–5.37	3.25–5.53
HGB (g/dL)	277	11.70–19.60	11.90–19.57	12.20–19.20	11.35–19.63
HCT (%)	277	33.79–56.11	34.20–55.83	35.20–54.21	33.22–55.74
MCV (fL)	277	92.59–111.63	92.83–110.97	93.86–109.61	92.37–110.49
MCH (pg)	277	31.59–38.81	32.04–38.70	32.59–38.11	31.99–38.55
MCHC (g/dL)	277	33.00–36.50	33.13–36.40	33.30–36.20	32.7–36.78
PLT (10³/ul)	277	118.60–413.15	128.68–408.60	154.70–390.10	137.18–411.74
RDW SD (fL)	277	50.60–73.51	50.87–72.73	52.47–70.57	49.29–70.61
RDW CV (%)	277	14.40–20.01	14.50–19.70	14.60–19.00	13.72–19.04
PDW (fL)	277	8.90–15.54	8.90–15.00	9.09–14.40	7.68–14.6
MPV (fL)	277	9.00–12.11	9.10–11.90	9.10–11.70	8.69–11.81
PLCR (%)	277	16.10–39.22	16.80–39.00	17.10–36.00	13.96–37.04
PCT (%)	277	0.13–0.40	0.14–0.40	0.17–0.38	0.16–0.4
Neutro (10³/uL)	277	3.47–21.37	3.67–20.91	3.94–19.83	1.72–20.32
Lymph (10³/uL)	277	2.51–6.78	2.57–6.74	2.64–6.18	2.03–6.43
Mono (10³/uL)	277	0.86–3.48	0.88–3.41	0.97–3.15	0.5–3.1
Eosinophils (10³/uL)	277	0.7–1.22	0.08–1.18	0.09–1.06	0–100
Eosinophils absolute (10³/uL)	277	1082.65–26356.28	1156.96–25602.86	1781.76–21922.39	0–100
Basophils (10³/uL)	277	0.02–0.18	0.02–0.17	0.03–0.16	0–0.16
Basophils absolute (10³/uL)	277	210.30–4544.55	221.98–4463.82	363.28–3821.85	0–100
Reticulocyte (10⁶/uL)	277	2.94–7.56	2.99–7.44	3.14–6.72	2.39–6.95

in narrative and table. Reference range P2.5–P97.5 means that 95% of normal individuals have normal laboratory results, while the other 5% may not be sick outside the normal limits. Reference range P3–P97 means that 94% of normal individuals have normal laboratory results, while the other 6% may not be sick outside the normal limits, in the same way for P5–P95 and mean ± 2SD.

Results

Two hundred and seventy-seven newborns met the inclusion and exclusion criteria, consisting of 145 (52.35%) male and 132 (47.65%) female infants.

The birth weight range, the birth length range, the head circumference range, and the chest circumference range are 2,500–4,450 g, 44.0–55.0 cm, 27.0–37.5 cm, and 26.0–37.5 cm, respectively. In addition, reference range of CBC and reticulocyte in healthy term newborns 1 week after birth is shown in Tables 1-3. Table 1 shows the reference range of CBC and reticulocyte from the 2.5th to 97.5th percentiles, 3th to 97th percentiles, 5th to 95th percentiles, and mean ±2SD for all newborns. Table 2 shows the reference range of CBC and reticulocyte from the 2.5th to 97.5th percentiles, 3th to 97th percentiles, 5th to 95th percentiles, and mean ± 2SD for male newborns. Finally, Table 3 shows the reference range of CBC and reticulocyte from the 2.5th to 97.5th percentiles, 3th to 97th percentiles, 5th to 95th percentiles, and mean ± 2SD for female newborns.

Table 2: Reference range of CBC and reticulocyte in healthy term male newborns 1 week after birth

CBC	n	$P_{2.5}$–$P_{97.5}$	P_3–P_{97}	P_5–P_{95}	Mean ± 2SD
WBC (10^3/uL)	145	8.52–30.69	8.71–29.13	9.32–24.62	6.36–25.76
RBC (10^6/uL)	145	3.41–5.63	3.42–5.57	3.59–5.42	3.35–5.59
HGB (g/dL)	145	12.20–20.14	12.28–19.91	12.63–19.38	11.47–20.15
HCT (%)	145	34.47–56.90	34.73–56.63	35.95–55.04	33.62–56.5
MCV (fL)	145	92.87–110.12	93.01–109.66	94.02–107.27	92.58–109.3
MCH (pg)	145	32.43–38.38	32.54–38.05	32.60–37.60	32.3–38.22
MCHC (g/dL)	145	32.96–36.54	33.24–36.50	33.33–36.37	32.53–37.21
PLT (10^3/ul)	145	101.55–424.05	106.66–419.20	132.80–396.20	124.93–408.77
RDW SD (fL)	145	50.57–72.41	50.75–72.22	52.73–70.50	49.44–69.92
RDW CV (%)	145	14.40–19.44	14.44–19.19	14.50–18.97	13.79–18.95
PDW (fL)	145	8.70–16.34	8.78–15.81	8.96–14.44	7.78–14.46
MPV (fL)	145	9.07–12.24	9.10–12.09	9.10–11.81	8.69–11.81
PLCR (%)	145	16.56–39.88	16.84–39.37	17.10–35.87	13.86–37.02
PCT (%)	145	0.12–0.40	0.12–0.40	0.16–0.38	0.15–0.39
Neutro (10^3/uL)	145	3.25–22.52	3.57–21.42	3.83–19.05	0.99–20.23
Lymph (10^3/uL)	145	2.44–6.79	2.51–6.73	2.60–6.10	1.94–6.22
Mono (10^3/uL)	145	0.86–3.28	0.87–3.17	0.98–2.97	0.57–2.93
Eosinophils (10^3/uL)	145	0.04–1.17	0.06–1.13	0.13–1.07	0–100
Eosinophils absolute (10^3/uL)	145	906.42–26162.07	1268.27–25587.84	1903.60–21988.33	0–100
Basophils (10^3/uL)	145	0.02–0.21	0.02–0.21	0.03–0.17	0–100
Basophils absolute (10^3/uL)	145	192.86–5055.90	209.16–4176.37	327.51–3746.19	0–100
Reticulocyte (10^6/uL)	145	2.70–7.06	2.83–7.02	2.99–6.58	2.3–6.5

11.47 g/dL, respectively. For female newborns, the P2.5, P3, P5, and mean-2SD values of Hb were 11.37 g/dL, 11.50 g/dL, 11.80 g/dL, or 11.37 g/dL, respectively.

By knowing the lower limit of the reference range of CBC and reticulocyte, we can determine ID and IDA with a combination of erythrocyte indices and peripheral blood smear. Determination of the CBC and reticulocyte reference range also helps establish a disease related to changes in the white blood counts value, platelets, basophils, eosinophils, neutrophil band, neutrophil segments, lymphocyte, monocytes, and reticulocyte, especially in newborns.

Keohane *et al.* obtained reference range of CBC data from Riley Hospital for Children, Indiana University

Table 3: Reference range of CBC and reticulocyte in healthy term female newborns 1 week after birth

CBC	n	$P_{2.5}$–$P_{97.5}$	P_3–P_{97}	P_5–P_{95}	Mean ± 2SD
WBC (10^3/uL)	132	7.83–31.00	8.01–30.21	8.100–28.71	7.47–29.03
RBC (10^6/uL)	132	3.10–5.49	3.15–5.48	3.23–5.27	3.15–5.47
HGB (g/dL)	132	11.37–19.20	11.50–19.20	11.80–19.20	11.37–18.93
HCT (%)	132	32.77–55.84	32.90–55.51	34.52–54.07	32.89–54.77
MCV (fL)	132	91.03–112.90	91.69–112.70	93.16–110.81	92.29–111.65
MCH (pg)	132	30.80–39.20	30.100–39.00	32.16–38.51	31.68–38.88
MCHC (g/dL)	132	33.00–36.20	33.00–36.20	33.20–36.10	32.97–36.21
PLT (10^3/ul)	132	133.58–402.00	140.89–402.00	188.65–390.35	152.33–413.33
RDW SD (fL)	132	49.92–75.47	50.79–75.20	52.17–71.76	49.15–71.35
RDW CV (%)	132	14.47–20.40	14.60–20.20	14.67–19.51	13.65–19.13
PDW (fL)	132	8.90–15.34	8.90–15.01	9.07–14.40	7.59–14.75
MPV (fL)	132	8.93–12.00	8.100–11.80	9.10–11.70	8.7–11.82
PLCR (%)	132	15.93–39.14	15.100–39.00	17.20–36.53	14.01–37.13
PCT (%)	132	0.16–0.41	0.17–0.40	0.20–0.38	0–100
Neutro (10^3/uL)	132	3.27–21.27	3.64–21.12	4.45–19.96	2.58–20.34
Lymph (10^3/uL)	132	2.55–6.87	2.63–6.78	2.67–6.25	2.16–6.64
Mono (10^3/uL)	132	0.87–3.91	0.88–3.75	0.92–3.37	0.45–3.25
Eosinophils (10^3/uL)	132	0.07–1.34	0.08–1.29	0.09–1.05	0–100
Eosinophils absolute (10^3/uL)	132	1037.23–28381.99	1152.27–26348.09	1547.16–21764.18	0–100
Basophils (10^3/uL)	132	0.02–0.17	0.02–0.17	0.03–0.16	0–0.16
Basophils absolute (10^3/uL)	132	262.20–4726.43	320.72–4532.91	398.65–4070.68	0–100
Reticulocyte (10^6/uL)	132	3.21–8.50	3.24–7.92	3.34–7.38	2.68–7.28

Health, Indianapolis. Hence, the lower limit value of the CBC is higher than the results of this study [15]. While The American Association of Pediatrics lists the reference range of CBC with P2.5–P97.5, the value is also higher than the results of this study [16]. This difference may be due to differences in genetics, race, ethnicity, parity, and nutritional/iron status of the mother.

Determining the lower limit of P2.5, P3, P5, or mean-2SD on examining specific parameters is commonly used statistically. For example, the WHO and CDC growth charts set the lower limit of weight-for-age, length/height-for-age, head circumference-for-age, and arm circumference-for-age at P3 [17]. Beutler *et al*. set the lower limit of Hb at P2.5 to state someone is anemic or not [18], while Goyette and Janus used the lower limit of P5 [19], [20]. Beutler stated that determining the lower limit of Hb with P2.5, or P5, of course, by considering race, ethnicity, age, gender, altitude above sea level [21]. Ariati *et al*. stated that the undernutrition and poor malnutrition were categorized into undernutrition status with a z-score <−2 SD [22]. Lotti *et al*. used the lower limit of the parameter is Mean±2SD, with the lower limit being <−2SD [23].

Conclusion

The advantage of this study is that it parades all CBC and reticulocyte reference range at P2.5–P97.5, P3–P97, P5–P95, and mean±2SD. Thus, the reference range of CBC and reticulocyte for healthy term newborns, male newborns, and female newborns in this study can be used as a benchmark. The limitation of this study is that the altitude, genetics, and the racial makeup of our population differ from populations in other areas of the world, and whether such differences are pertinent to CBC and reticulocyte parameters of neonates are not known. In the future, the methods of this study can be adapted to examine other markers of anemia (ferritin, sTfR, transferrin saturation, and C-reactive protein) to assist a more reliable diagnosis.

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