RESEARCH ARTICLE

Establishment of reference intervals for complete blood count parameters during normal pregnancy in Beijing

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Objective: To observe the changes of complete blood count (CBC) parameters during pregnancy and establish appropriate reference intervals for healthy pregnant women.

Methods: Healthy pregnant women took the blood tests at all trimesters. All blood samples were processed on Sysmex XE-2100. The following CBC parameters were analyzed: red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), white blood cell count (WBC), and leukocyte differential count. Reference intervals were established using the 2.5th and 97.5th percentile of the distribution.

Results: Complete blood count parameters showed dynamic changes during trimesters. RBC, Hb, Hct declined at trimester 1, reaching their lowest point at trimester 2, and began to rise again at trimester 3. WBC, neutrophil count (Neut), monocyte count (MONO), RDW, and PDW went up from trimester 1 to trimester 3. On the contrary, MCHC, lymphocyte count (LYMPH), PLT, and MPV gradually descended during pregnancy. There were statistical significances in all CBC parameters between pregnant women and normal women, regardless of the trimesters ($P < .001$). The median obtained were (normal vs pregnancy) as follows: RBC 4.50 vs $3.94 \times 10^{12}/L$, Hb 137 vs 120 g/L, WBC 5.71 vs $9.06 \times 10^9/L$, LYMPH% 32.2 vs 18.0 , Neut% 58.7 vs 75.0 , and PLT 251 vs $202 \times 10^9/L$.

Conclusion: The changes of CBC parameters during pregnancy are described, and reference intervals for Beijing pregnant women are demonstrated in this study.

KEYWORDS

complete blood count, pregnancy, reference interval

1 | INTRODUCTION

Complete blood count (CBC) has evolved into the typical test panel today, including assessment of WBCs, RBCs, and platelets.¹ Although CBC has been found to be a poor indicator for screening the undetected disease in the asymptomatic members of the general population, it provides such valuable information about a patient's or

pregnant woman's physiologic status.²⁻⁴ During pregnancy, a lot of physiologic changes occur to accommodate the demands of the developing fetus, which affects the hematologic parameters directly or indirectly. These hematologic changes are considered to be the risk factors affecting maternal and pregnancy outcome.⁵⁻⁸ For hematologic complication that can be discriminated and treated early, it is important to know the variation during the entire stages of pregnancy. Thus, to understand the changes better and distinguish whether it caused by physiologic or pathologic, there is a basic need

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to update reference intervals of CBC for pregnant women. Studies based on other ethnicities had been reported previously, but it may not be applicable for Chinese.⁹⁻¹¹ As researches reported about Chinese women are rare, we designed this investigation to observe the dynamic changes of CBC parameters during pregnancy and establish appropriate reference intervals for healthy Beijing Chinese pregnant women.

2 | METHODS

2.1 | Ethics approval

This study was approved by the ethics committee of Peking University Third Hospital.

2.2 | Subject selection

Pregnant women were chosen from the department of gynecology and obstetrics, and nonpregnant women were randomly selected as the control group from the medical examination center of Peking University Third Hospital. Inclusion criteria were as follows: Chinese woman with 18-46 years age, live in Beijing more than 5 years. The evaluation of health status and exclusion criteria was referred to the previous study.^{12,13} Besides, pregnant women with any of the following conditions were excluded: pregnancy associated with cardiac disease, pregnancy-induced hypertension syndrome, pregnancy associated with diabetes, intrahepatic cholestasis of pregnancy, and pregnancy associated with hysteromyoma.

2.3 | Sample collection

Blood samples (3 mL) were collected by plastic whole blood tube with spray-coated K₂EDTA (Becton Dickinson Medical Devices Co Ltd, NC, USA) in a standard procedure of venous blood collection at trimester 1 (1-12 weeks of gestation), trimester 2 (13-27 weeks of gestation), and trimester 3 (28-40 weeks of gestation), respectively.

2.4 | Laboratory analysis

Complete blood count, including red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), white blood cell count (WBC), and leukocyte differential count, was processed by Sysmex XE-2100 (Sysmex Corporation, Kobe, Japan). The hematology analyzer was calibrated and maintained according to the manufacture's instruction. Three levels of quality control were made twice every day to ensure the good precision. Every sample was tested on the analyzer within 1 hour.

2.5 | Statistics

According to CLSI document CA28-A3c,¹⁴ reference intervals were established using the 2.5th and 97.5th percentile of the distribution. The ratio D/R proposed by Dixon was adopted to exclude outliers. Nonparametric procedure was used to determine statistical significance. $P < .05$ was considered to represent a significant difference. All statistical calculations were performed in SPSS 20.0 (SPSS Inc., Chicago, IL, USA).

3 | RESULTS

3.1 | Reference individuals

Three thousand and sixty pregnant women fulfilled the criteria were enrolled between July 2014 and December 2014, including 1193 women at trimester 1 (1-12 weeks of gestation), 698 at trimester 2 (13-27 weeks of gestation), and 1169 at trimester 3 (28-40 weeks of gestation). All of them were apparently healthy with a normal pregnancy. The characteristics of the inclusive women are shown in Table 1. Four hundred and eighty-three nonpregnant women were included in the control group.

TABLE 1 Characteristics of the inclusive women in this study

Characteristics	Nonpregnant women	Pregnant women		
		Trimester 1	Trimester 2	Trimester 3
No.	483	1193	698	1169
Age (y)	34±7	32±4	33±5	32±4
Glucose (mmol/L)	5.06±0.58	4.90±0.45	5.07±0.84	5.12±1.32
Alanine aminotransferase (U/L)	15±10.21	13±6.64	12±6.14	11±6.25
Aspartate aminotransferase (U/L)	18±4.89	19±3.97	21±5.14	21±4.89
Urea (mmol/L)	4.3±1.03	3.3±0.79	3.5±1.29	3.8±1.80
Creatinine (μmol/L)	57±7.15	59±6.69	54±11.77	56±14.30
Uric acid (μmol/L)	252±58.91	218±45.69	228±54.62	246±56.75

Data are presented as mean±SD.

3.2 | Reference intervals

The median of CBC parameters for normal and pregnant women was compared as shown in Table 2, and reference intervals of each trimester for RBCs, WBCs, and platelets are shown in Table 3. Reference limits were calculated as the 2.5th and 97.5th percentile of these CBC parameters.

3.3 | Erythrocyte indices

Red blood cell, Hb, Hct declined at trimester 1, reaching their lowest point at trimester 2, and began to rise again at trimester 3, see Figure 1. The median of RBC at trimester 2 was $3.75 \times 10^{12}/L$. Highly significant association existed between Hb and Hct ($r_{T1}=.928$, $P<.0001$; $r_{T2}=.964$, $P<.0001$; $r_{T3}=.970$, $P<.0001$), both of whom have a correlation with RBC at all trimesters ($P<.0001$). The median of Hb and Hct at trimester 2 was 115 g/L and 0.34, respectively. Hb values <110 g/L were found in 2% (29/1193) of the women at trimester 1, in 29% (204/698) at trimester 2, and in 31%(359/1169) at trimester 3.

Mean corpuscular volume dropped at trimester 1 ($P<.0001$), then gradually went back to the normal level at trimester 2, see Figure 2. Mean corpuscular volume values <80 fL were observed in 4% of the women during pregnancy. MCH fell slightly at trimester 1 ($P<.0001$),

TABLE 2 Comparison of complete blood count parameters between normal and pregnant women

Group	Normal	Pregnancy	P
RBC, $10^{12}/L$	4.50	3.94	***
Hb, g/L	137	120	***
Hct	0.42	0.36	***
MCV, fL	91.8	90.8	**
MCH, pg	30.3	30.5	**
MCHC, g/L	330	336	***
RDW, %	12.3	13.5	***
WBC, $10^9/L$	5.71	9.06	***
LYMPH, %	32.2	18.0	***
LYMPH, $10^9/L$	1.84	1.60	***
Neut, %	58.7	75.0	***
Neut, $10^9/L$	3.31	6.72	***
EO, %	1.3	0.6	***
EO, $10^9/L$	0.08	0.05	***
BASO, %	0.5	0.2	***
BASO, $10^9/L$	0.03	0.01	***
MONO, %	6.3	5.3	***
MONO, $10^9/L$	0.36	0.50	***
PLT, $10^9/L$	251	202	***
MPV, fL	10.6	9.7	***
PDW, fL	12.3	16.2	***

Data are presented as median.

** $P<.001$, *** $P<.0001$ between the normal and pregnant women groups.

mounting at trimester 2, and dropped again at trimester 3 ($P=.031$). Values of MCH <27 pg were observed in 4% of the pregnant women. MCHC went up at trimester 1 and gradually declined from trimester 1 to trimester 3 ($P<.0001$). None of the women had values of MCHC <300 g/L in this study. RDW climbed from trimester 1 to trimester 3 ($P<.0001$). Values of RDW $>15\%$ were observed in 5%, 6% of the women at trimester 1, and trimester 2, respectively, and were observed in 21% at trimester 3.

3.4 | Leukocyte indices

White blood cell was mounting during all trimesters ($P<.0001$), see Figure 3. But there was no significant difference between trimester 2 and trimester 3. The median of WBC at trimester 3 was $9.60 \times 10^9/L$.

In leukocyte differential count, lymphocyte count (LYMPH) was on a decline during pregnancy ($P<.0001$), see Figure 3. Meanwhile, neutrophil count (Neut) and monocyte count (MONO) were going up ($P<.0001$). Highly significant correlation existed between WBC and Neut during pregnancy ($r_{T1}=.959$, $P<.0001$; $r_{T2}=.971$, $P<.0001$; $r_{T3}=.978$, $P<.0001$). As WBC, Neut had no significant difference between trimester 2 and trimester 3, either.

3.5 | Platelet indices

Platelet descended gradually during pregnancy ($P<.0001$), see Figure 4. The median of PLT at trimester 3 was $187 \times 10^9/L$. MPV was going down, and PDW was going up from trimester 1 to trimester 3 ($P<.0001$).

4 | DISCUSSION

Complete blood count is examined all over the world to assess a patient's physiologic status, as it is not only a reliable but also simple, fast, and cost-effective test. During pregnancy, changes occur and can be observed in CBC. Some of the parameters are decreased like Hb and PLT, and others are increased like WBC.^{10,11,15} The aim of the study was to describe the variation of CBC during pregnancy and determine the appropriate reference intervals for pregnant women.

Anemia in pregnancy is the most common hematologic problem concerned by the doctors.¹⁶ Since 1968, WHO suggested that anemia in pregnancy was likely to be present when Hb was <110 g/L.¹⁷ In our study, we found Hb had a decline during trimester 1, reaching the lowest point at trimester 2 and began to rise again at trimester 3, which was similar with previous studies.^{18,19} One reason for this phenomenon may be the secondary hemodilution to an increase in plasma volume, which is known as physiologic anemia.²⁰ During pregnancy, physiologic changes are mainly influenced by changes in the hormonal environment. The additional progesterone and estrogen that are secreted by the placenta cause a release of renin from kidneys. Renin stimulates the aldosterone–renin–angiotensin mechanism, leading to sodium retention and increased plasma volume. Plasma volume begins to increase as early as 6 weeks of gestation and increase to more

TABLE 3 Reference intervals for complete blood count parameters during pregnancy

Variables	Trimester 1		Trimester 2		Trimester 3	
	2.5th	97.5th	2.5th	97.5th	2.5th	97.5th
RBC, $10^{12}/L$	3.70 (3.63-3.72)	5.07 (5.05-5.15)	2.85 (2.76-2.98)	4.59 (4.43-4.68)	2.75 (2.68-2.90)	4.64 (4.62-4.76)
Hb, g/L	110 (105-110)	147 (147-149)	88 (85-91)	136 (134-138)	84 (83-87)	141 (139-143)
Hct	0.33 (0.32-0.33)	0.43 (0.43-0.44)	0.27 (0.25-0.27)	0.40 (0.39-0.40)	0.26 (0.25-0.26)	0.42 (0.41-0.42)
MCV, fL	76.8 (71.3-77.2)	95.2 (95.1-95.9)	78.3 (73.6-83.1)	99.7 (98.9-100.5)	78.7 (73.9-79.5)	101.7 (101.5-102.6)
MCH, pg	24.6 (22.2-25.2)	32.7 (32.6-33.2)	24.6 (23.1-27.1)	34.0 (33.7-34.4)	25.1 (23.3-25.2)	34.6 (34.4-34.8)
MCHC, g/L	320 (316-320)	355 (355-357)	319 (315-321)	351 (350-352)	315 (310-315)	348 (347-349)
RDW, %	11.9 (11.8-11.9)	16.8 (16.4-18.0)	12.3 (12.2-12.4)	17.2 (16.5-18.5)	12.3 (12.2-12.3)	19.8 (19.3-20.5)
WBC, $10^9/L$	4.68 (4.45-4.78)	12.87 (12.74-13.46)	5.97 (5.77-6.20)	16.78 (16.00-18.35)	5.53 (5.40-5.90)	19.56 (18.90-21.60)
LYMPH, %	13.4 (11.8-13.7)	40.2 (39.6-41.6)	7.3 (6.0-8.4)	29.4 (28.4-30.9)	4.4 (3.4-4.5)	29.7 (28.8-32.2)
LYMPH, $10^9/L$	1.11 (1.01-1.12)	3.05 (3.00-3.20)	0.86 (0.75-0.90)	2.88 (2.70-3.15)	0.70 (0.50-0.70)	2.60 (2.51-2.87)
Neut, %	52.8 (50.9-53.4)	81.6 (81.3-83.2)	62.7 (60.3-63.8)	87.6 (86.2-90.4)	61.7 (58.5-63.2)	91.9 (91.9-93.6)
Neut, $10^9/L$	2.72 (2.49-2.78)	9.92 (9.78-10.29)	4.16 (3.82-4.34)	14.11 (13.00-15.41)	3.73 (3.57-3.90)	17.24 (16.70-20.20)
EO, %	0.1 (0.1-0.1)	4.1 (3.9-4.5)	0.0 (0.0-0.1)	3.7 (3.0-4.5)	0.0 (0.0-0.0)	2.7 (2.4-3.1)
EO, $10^9/L$	0.01 (0.00-0.01)	0.31 (0.29-0.34)	0.00 (0.00-0.00)	0.35 (0.30-0.40)	0.00 (0.00-0.00)	0.23 (0.20-0.29)
BASO, %	0.1 (0.0-0.1)	0.6 (0.6-0.7)	0.0 (0.0-0.0)	0.5 (0.5-0.6)	0.0 (0.0-0.0)	0.6 (0.5-0.6)
BASO, $10^9/L$	0.00 (0.00-0.00)	0.05 (0.04-0.05)	0.00 (0.00-0.00)	0.07 (0.06-0.10)	0.00 (0.00-0.00)	0.10 (0.07-0.10)
MONO, %	3.0 (2.8-3.0)	7.9 (7.8-8.3)	2.7 (2.6-2.9)	8.8 (8.3-9.2)	2.4 (1.8-2.4)	9.7 (9.5-10.3)
MONO, $10^9/L$	0.20 (0.19-0.21)	0.66 (0.65-0.69)	0.22 (0.20-0.25)	0.98 (0.90-1.10)	0.26 (0.20-0.27)	1.10 (1.03-1.16)
PLT, $10^9/L$	148 (140-152)	352 (343-362)	111 (105-115)	346 (329-370)	80 (78-93)	309 (309-340)
MPV, fL	8.5 (7.9-8.7)	11.9 (11.9-12.2)	7.0 (6.7-7.2)	11.8 (11.6-11.9)	7.0 (6.8-7.1)	12.9 (12.6-13.2)
PDW, fL	9.0 (8.9-9.1)	16.4 (16.3-16.9)	9.1 (8.8-9.2)	18.1 (17.9-18.5)	10.2 (9.6-10.2)	19.1 (18.9-19.3)

FIGURE 1 Red blood cell, Hb, and Hct during pregnancy. The dots reflect the median, and the bars reflect the lower and upper limit using the 25th and 75th percentiles. N: normal; T1: trimester 1; T2: trimester 2; T3: trimester 3

than 50% of the progestation level,²¹ mainly to content the demands of the new vascular bed and to guard against blood loss occurring at delivery.²² However, red cell mass, which driven by an increase in maternal erythropoietin production, also increases during pregnancy, but relatively less than plasma volume,²³ which results in a fall in maternal RBC and Hb. But at trimester 3, there is a rise in Hb and Hct, when the ascent of plasma volume at a slower rate owing to an increase of atrial natriuretic peptide.²⁴

Moreover, the decline in Hb during pregnancy may be due to an increased demand for iron. More iron is required to meet the expansion of maternal Hb and the needs of fetal growth, but the iron required is usually inadequate from the dietary intake.^{25,26} In our study, although each pregnant woman was directed to take a vitamin-mineral supplement containing 60 mg ferrous iron/day for prophylaxis as

recommended,²⁵ values of Hb <110 g/L had been found in approximately 30% of the women at trimester 2 and trimester 3, respectively. But according to the diagnosis of iron deficiency anemia using MCV <80 fL and MCH <27 pg,²⁷ there were only 4% or less pregnant women of our study who maybe had a risk of anemia. MCHC is a mathematical calculation dependent on Hct and Hb. In healthy non-pregnant women, MCHC <300 is coincidental with an anemia which may be caused by iron deficiency.²⁷ None of the women of our study had values of MCHC <300 g/L during pregnancy, although it has been stated that MCHC is of no use during pregnancy due to the great interindividual variation in the degree of hemodilution.²⁸ Although a rising RDW is a hint for iron deficiency anemia, it consisted in the erythropoiesis during pregnancy. Thus, we suggest that for pregnant Chinese women, Hb <110 g/L should not as the key diagnostic code

FIGURE 2 Mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and red blood cell distribution width during pregnancy. The dots reflect the median, and the bars reflect the lower and upper limit using the 25th and 75th percentiles. N: normal; T1: trimester 1; T2: trimester 2; T3: trimester 3

FIGURE 3 White blood cell, lymphocyte, Neut, and monocyte during pregnancy. The dots reflect the median, and the bars reflect the lower and upper limit using the 25th and 75th percentiles. N: normal; T1: trimester 1; T2: trimester 2; T3: trimester 3

FIGURE 4 Platelet, mean platelet volume, and platelet distribution width during pregnancy. The dots reflect the median, and the bars reflect the lower and upper limit using the 25th and 75th percentiles. N: normal; T1: trimester 1; T2: trimester 2; T3: trimester 3

for anemia, meanwhile the iron status situation must be monitored closely by means of MCV, MCH, MCHC, and serum ferritin, especially at trimester 2 and trimester 3.

The leukocytosis is due to increased inflammatory response during pregnancy, which can be as a consequence of selective immune tolerance, immunosuppression, and immunomodulation of fetus.²⁹

In our study, there was a significant rise in WBC during pregnancy, which is consistent with other findings.^{11,19,30} The median of WBC for normal women in this study was $5.71 \times 10^9/L$, and the value was greatly surpassed by the women during pregnancy, whose median was $9.06 \times 10^9/L$. In our study, it also showed that the increase in WBC is predominantly caused by an increase in granulocyte count with

neutrophils as the major type. The increase in granulocytes or neutrophils may represent a response to the physiologic stress induced by the pregnant state due to redistribution of WBCs between the marginal and circulating pools³¹ or impaired neutrophil apoptosis.³² Pain, nausea, vomiting, and anxiety, which one woman would experience all of them during pregnancy, have been reported to cause leukocytosis in the absence of infection.³³ In the peripheral blood film, immature forms as myelocytes and metamyelocytes were found in 22% of pregnant women at trimester 2 and trimester 3, none at trimester 1. Neutrophil band forms $\geq 5\%$ were found in 69% of pregnant women at all trimesters. As there is no pathological significance, we supposed that they just simply indicate adequate bone marrow response to an increased drive for erythropoiesis occurring during pregnancy.

Gestational thrombocytopenia is the second common hematologic problem consulting the doctors.³⁴ It is usually secondary to physiologic changes during gestation, namely platelet activation and increased platelet clearance.³⁴ Thrombocytopenia is classically defined as $PLT < 150 \times 10^9/L$.¹¹ In our study, a gradual reduction in PLT count was shown during pregnancy and $PLT < 150 \times 10^9/L$ was observed in 3%, 12%, and 23% of the women at trimester 1, 2, and 3, respectively. But there was no pathological significance. PDW increased continuously during pregnancy, which made MPV become an insensitive measurement of the platelet size. In our study, gestational thrombocytopenia requires no specific treatment and corrects itself spontaneously after delivery but is of importance to distinguish from other diseases like immune thrombocytopenia and megaloblastic anemia.³⁵

5 | CONCLUSION

The changes of CBC parameters during pregnancy are described in this study. There are significant differences between pregnant women and nonpregnant. These results may be helpful in the evaluation of the health status for pregnant women and could be applied to every region with the similar ethnic and economic situation. The present values could be good resources to update reference intervals for healthy pregnancy.

REFERENCES

- Rodak BF, Fritsma GA, Keohane E. *Hematology: Clinical principles and applications*, 4th edn. Philadelphia, PA: Saunders; 2011.
- Dixon LR. The complete blood count: physiologic basis and clinical usage. *J Perinat Neonatal Nurs*. 1997;11:1–18.
- Shapiro MF, Greenfield S. The complete blood count and leukocyte differential count. An approach to their rational application. *Ann Intern Med*. 1987;106:65–74.
- Carraro P, Vettore G, Padoan A, Piva E, Plebani M. Complete blood count at the ed: preanalytic variables for hemoglobin and leukocytes. *Am J Emerg Med*. 2015;33:1152–1157.
- Rukuni R, Bhattacharya S, Murphy MF, Roberts D, Stanworth SJ, Knight M. Maternal and neonatal outcomes of antenatal anemia in a scottish population: a retrospective cohort study. *Acta Obstet Gynecol Scand*. 2016;95:555–564.
- Zhang Y, Jin L, Liu JM, Ye R, Ren A. Maternal hemoglobin concentration during gestation and risk of anemia in infancy: secondary analysis of a randomized controlled trial. *J Pediatr*. 2016;175:106–110. e2
- Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr*. 2016;103:495–504.
- Sharma S, Sidhu H, Kaur S. Analytical study of intrauterine fetal death cases and associated maternal conditions. *Int J Appl Basic Med Res*. 2016;6:11–13.
- Harm SK, Yazer MH, Waters JH. Changes in hematologic indices in Caucasian and non-Caucasian pregnant women in the United States. *Korean J Hematol*. 2012;47:136–141.
- Milman N, Bergholt T, Byg K-E, Eriksen L, Hvas A-M. Reference intervals for haematological variables during normal pregnancy and postpartum in 434 healthy danish women. *Eur J Haematol*. 2007;79:39–46.
- Akinbami AA, Ajibola SO, Rabiun KA, et al. Hematological profile of normal pregnant women in Lagos, Nigeria. *Int J Womens Health*. 2013;5:227–232.
- Yang S, Qiao R, Li ZR, et al. Establishment of reference intervals of 24 chemistries in apparently healthy adult han population of northern china. *Clin Biochem*. 2012;45:1213–1218.
- Qiao R, Yang S, Yao B, Wang HY, Zhang J, Shang H. Complete blood count reference intervals and age- and sex-related trends of north china han population. *Clin Chem Lab Med*. 2014;52:1025–1032.
- CLSI. *Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline*, 3rd edn. CLSI document C28-A3c. Horowitz GL. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
- Rizack T, Rosene-Montella K. Special hematologic issues in the pregnant patient. *Hematol Oncol Clin North Am*. 2012;26:409–432. x.
- Krafft A, Murray-Kolb L, Milman N. Anemia and iron deficiency in pregnancy. *J Pregnancy*. 2012;2012:241869.
- World Health Organization. Nutritional anaemias. Report of a WHO scientific group. Geneva, 1968. (WHO Technical Report Series, No.405). http://whqlibdoc.who.int/trs/WHO_TRS_405.pdf
- Jwa SC, Fujiwara T, Yamanobe Y, Kozuka K, Sago H. Changes in maternal hemoglobin during pregnancy and birth outcomes. *BMC Pregnancy Childbirth*. 2015;15:80.
- Miri-Dashe T, Osawe S, Tokdung M, et al. Comprehensive reference ranges for hematology and clinical chemistry laboratory parameters derived from normal nigerian adults. *PLoS ONE*. 2014;9:e93919.
- Horowitz KM, Ingardia CJ, Borgida AF. Anemia in pregnancy. *Clin Lab Med*. 2013;33:281–291.
- Lund CJ, Donovan JC. Blood volume during pregnancy. Significance of plasma and red cell volumes. *Am J Obstet Gynecol*. 1967;98:394–403.
- Margaret R. Normal hematological changes during pregnancy and the puerperium. In: Pavord S, Hunt B, eds. *The Obstetric Hematology Manual*. Cambridge: Cambridge University Press; 2010:1–11.
- Taylor DJ, Lind T. Red cell mass during and after normal pregnancy. *Br J Obstet Gynaecol*. 1979;86:364–370.
- Chapman AB, Abraham WT, Zamudio S, et al. Temporal relationships between hormonal and hemodynamic changes in early human pregnancy. *Kidney Int*. 1998;54:2056–2063.
- Milman N. Oral iron prophylaxis in pregnancy: not too little and not too much!. *J Pregnancy*. 2012;2012:514345.
- Di Renzo GC, Spano F, Giardina I, Brillo E, Clerici G, Roura LC. Iron deficiency anemia in pregnancy. *Womens Health*. 2015;11:891–900.
- Roberts WE, Morrison JC. Evaluation of anemia in pregnancy. In: Kitay DZ, ed. *Hematologic Problems in Pregnancy*. Oradell: Medical Economics Books; 1987:15–26.
- Cabaniss CD, Cabaniss ML. Physiologic hematology of pregnancy. In: Kitay DZ, ed. *Hematologic Problems in Pregnancy*. Oradell: Medical Economics Books; 1987:3–14.

29. Kaur S, Khan S, Nigam A. Hematological profile and pregnancy: a review. *Int J Adv Med*. 2014;1:1.
30. Efrati P, Presentey B, Margalith M, Rozenszajn L. Leukocytes of normal pregnant women. *Obstet Gynecol*. 1964;23:429–432.
31. Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. *Indian J Hematol Blood Transfus*. 2012;28:144–146.
32. von Dadelszen P, Watson RW, Noorwali F, et al. Maternal neutrophil apoptosis in normal pregnancy, preeclampsia, and normotensive intra-uterine growth restriction. *Am J Obstet Gynecol*. 1999;181:408–414.
33. Milhorat AT, Small SM, Diethelm O. Leukocytosis during various emotional states. *Arch Neurol Psychiatry*. 1942;47:779–792.
34. Townsley DM. Hematologic complications of pregnancy. *Semin Hematol*. 2013;50:222–231.
35. Myers B. Diagnosis and management of maternal thrombocytopenia in pregnancy. *Br J Haematol*. 2012;158:3–15.

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