Original Article

The relationship of hemoglobin and hematocrit in the first and second half of pregnancy with pregnancy outcome

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Abstract

Background: Considering the relationship of low and high levels of hemoglobin and hematocrit with some pregnancy complications, we decided to study their relationship with pregnancy outcome. This study also aimed to investigate the changes in hemoglobin and hematocrit values during the second and first half of pregnancy and its relationship with pregnancy outcome.

Materials and Methods: In a prospective cohort study, 520 Iranian pregnant women, aged 15 to 45 years that were supported by health centers in Isfahan, Iran, were recruited using quota sampling method. Exclusion criteria comprised of 36 conditions that were related to the maternal and infant outcomes. Hemoglobin and hematocrit were measured in eligible mothers during the 6th-11th weeks and 26th-30th weeks of pregnancy. They were monitored until delivery and the data regarding their pregnancy outcome were collected.

Findings: Low levels of hemoglobin during the first half of pregnancy was associated with preeclampsia (p = 0.024). Moreover, low levels of hemoglobin during the second half of pregnancy was associated with the risk of preterm premature rupture of membranes (p = 0.01). In addition, mothers with lower blood dilution, as a physiological process during pregnancy, were more prone to preeclampsia (p = 0.04).

Conclusions: Hemoglobin levels in the first and second half of pregnancy can predict preeclampsia and premature preterm rupture of membranes. Increased hematocrit levels in the second half of pregnancy or lack of reduction of hematocrit levels in the second half compared to the first half can estimate preeclampsia.

Key words: Hemoglobin, hematocrit, pregnancy outcome

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Introduction

In the past three decades, the relationship between maternal hemoglobin and hematocrit levels and pregnancy outcome has been generally studied. Maternal anemia has been considered as a risk factor for an undesirable pregnancy outcome.[1-3] On the other hand, the relationship between high levels of hemoglobin and hematocrit and the complications such as preterm delivery, low birth weight, intrauterine growth restriction and intrauterine fetal death have been also shown in several studies.[4-7] According to the study of Stove et al. conducted on Bulgarian pregnant women, increase of hematocrit, hemoglobin and red cell mass in early pregnancy can be considered a risk factor for preeclampsia, intrauterine growth restriction and fetal death in the later stages of pregnancy.[8]

Measuring hemoglobin and hematocrit is common during pregnancy. Normal level of hemoglobin is 12 to 16 grams per deciliter for women of childbearing age. Its minimum normal value is 11 grams per deciliter in the first and third trimester of the pregnancy and 10.5 grams per deciliter in

the second trimester. Its amount gets lower than normal due to anemia and higher than normal because of erythrocytosis. Normal values of hematocrit have been determined from 36 to 48 percent for women in childbearing age. The cause of its decrease in adults and during pregnancy is anemia, and the reasons for its increase are myeloproliferative disorders, chronic obstructive pulmonary disease and other hypoxic lung conditions.

Both hemoglobin and hematocrit are measured through fresh whole blood and are dependent on plasma volume. Thus, factors such as dehydration as well as overhydration can affect the test results.[9] In fact, hematocrit is a more precise parameter than hemoglobin to determine the ratio of erythrocyte volume to the total blood volume.[10] Viscosity of blood is changeable, which is associated with geometry of blood vessels and blood flow level, blood plasma concentration, volume concentration of blood cells and hematocrit. Therefore, change in the mentioned parameters can be a warning of a high-risk pregnancy.[11] The relationship between ferritin level and pregnancy outcome as well as the relationship between the hematocrit levels provide grounds for more investigation especially considering that such a study has not yet been done in Iran.[12,13] Our purposes were to examine the relationship of hemoglobin and hematocrit during the first and second half of pregnancy with pregnancy outcome including premature rupture of membranes (PROM) before the onset of labor, preterm premature rupture of membranes (PPROM) before completion of the thirty-seventh week of pregnancy, preeclampsia, delivery type and birth anthropometric indicators. We also aimed to study the changes in hemoglobin and hematocrit values during the second half of pregnancy compared to the first half and its relationship with pregnancy outcome.

Materials And Methods

In a prospective cohort study that was conducted on 520 pregnant women, the data were collected in three stages. Sampled population was Iranian women aged 15- 49 years covered by health centers whose delivery in hospital led to the birth of alive and apparently healthy baby. Subjects were selected from different centers through quota sampling method. Considering the possibility of loss to follow up and exclusion of the subjects whose babies suffered from abnormality, intrauterine fetal death and newborn death, a larger sample size (about 50) was determined. Exclusion criteria (36 items) were conditions and states that affect pregnancy outcome. These condition included causes of preterm delivery, low birth weight, preeclampsia, premature rupture of membranes, preterm premature rupture of membranes, smoking, drug addiction, digestive disorders, hemoglobinopathies, nutritional diseases, allergies and mental disorders. To determine the mentioned criteria, the results of the routine tests during pregnancy as well as the result obtained by the medical examination of the physician and the recommendation of the specialist in necessary cases were used. Pregnant women with gestational age of 6 weeks or less were interviewed in their first visit for prenatal care and in case they were eligible and willing to participate in the study, they were recruited. The participants were referred to the laboratory during the 6th-11th and 26th-30th weeks of gestational age and their hemoglobin and hematocrit were measured. It should be noted that 96 percent of the subjects took iron and folic acid pills. However, in order to increase the confidence in the study, all patients were referred to the same laboratory and all the samples were evaluated by the same technician. Further, the subjects were monitored until the delivery and the data regarding their pregnancy outcome were collected through birth files, prenatal care files and phone calls. Data collection tool was questionnaires which were completed through interviews with eligible mothers either in person or by phone call. Content validity of the questionnaire was confirmed by experts. The data in the prenatal care and delivery files which had been completed by midwives, obstetricians, and neonatologists were used to determine the reliability of the questionnaire. Student's t-test, Pearson correlation test and regression analysis was used to analyze the data through SPSS software version 18. Numerical values were represented as mean (standard deviation).

Findings

Pregnant women were at 15-41 years age group and their education was at the secondary level in 45.7 percent of cases and about 60 percent of pregnant women were experiencing their first pregnancy. Hemoglobin in the first half of pregnancy was 12.61 (1.06) g/dL and average hematocrit in the first half of pregnancy was 38.19 (3.07) grams percent. Hemoglobin in the second half of pregnancy was 11.91 (1.02) g/dL and average hematocrit was 36.28 (2.81) g/dl. Minimum and maximum amounts of hemoglobin were 7.4 and 16.1 g/dL in the first half and 7 and 15 g/dL in the second half, respectively. Moreover, the minimum and maximum values of hematocrit in the first half were calculated*as* 26 and 48.7 percent and in the second half as 27 and 46 percent, respectively. The average hemoglobin and hematocrit in

two halves of pregnancy in women who were affected with premature rupture of membranes (before the onset of labor and after 37 weeks) were not different with other mothers. Furthermore, there was no statistically significant difference in the average hemoglobin and hematocrit in two halves of pregnancy between those who had vaginal delivery and cesarean section (Table 1). Moreover, no relationship was found between hemoglobin in two halves of pregnancy and birth anthropometric indices ($p > 0.05$).

In the present study, about 2.35 percent of participants affected with preterm premature rupture of membranes and the average hemoglobin in the first and average hematocrit in the second half did not differ in both groups. However, the average hemoglobin in the second half of pregnancy of the group who later developed preterm premature rupture of membranes was significantly lower than others ($p = 0.01$). About 4 percent of subjects had signs and symptoms of preeclampsia. Average hemoglobin in the first half of pregnancy of these women was significantly more than that of others ($p = 0.024$) (Table 1). Significant inverse relationship of hematocrit in the second half with height ($p = 0.024$ and $r = -0.093$) and weight ($p = 0.03$ and $r = -0.095$) at birth was seen, so that the increase of hematocrit in the second half of pregnancy, correlated with decreased birth weight and height, but no significant relationship was found between head circumference at birth, and hemoglobin or hematocrit in the two halves ($p > 0.05$). Since the most important factor associated with indices of weight, height and head circumference at birth is gestational age, mentioned variables will be also influenced by some variables such as mother's age, education and body mass index, the number of pregnancies and household income. The relationship of hematocrit in the second half with birth weight and height was examined through a more accurate test using regression analysis while household income, mother's education and age, gestational age, maternal body mass index before pregnancy and the number of pregnancies were included in the model. No statistically significant relationship was found between hematocrit in the second half and birth weight and height ($p = 0.181$ and $p = 0.244$, respectively). But a significant relationship was found between gestational age ($p < 0.001$), mother's body mass index ($p = 0.001$), and education ($p = 0.021$), and birth weight. Moreover, a significant correlation was found between gestational age ($p < 0.001$), mothers' age ($p = 0.01$), mothers' education ($p < 0.001$), and birth height . In addition, gestational age ($p < 0.001$), maternal age ($p = 0.01$), and mother's education ($p < 0.001$) were significantly associated with head circumference at birth. Thus, among the mentioned variables, gestational age was strongly associated with the three infant anthropometric indices ($p < 0.001$).

To study the changes in hemoglobin and hematocrit values in the second half of pregnancy compared to the first half, the difference between hemoglobin and hematocrit in the two halves of pregnancy was determined for all of mothers. In 381 (72.9%) mothers, hemoglobin and hematocrit levels in the second half of pregnancy decreased to the first half of pregnancy and in 141 (27.0%), the difference between hematocrit in the two halves of pregnancy was zero or higher. In the next step, the relationship of the difference between hemoglobin and hematocrit in the two halves of pregnancy was assessed with premature rupture of membranes and preterm premature rupture of membranes, delivery type, preeclampsia, and gestational age. The difference between hematocrit in the two halves was inversely associated with gestational age ($p = 0.006$, $r = -0.21$). In addition, no significant relationship was found in terms of the hematocrit and hemoglobin differences in the two halves of pregnancy with premature rupture of membranes, preterm premature rupture of membranes and delivery type ($p > 0.05$). However, the difference between hematocrit in the two halves of pregnancy was significantly less in those who were diagnosed with preeclampsia than other mothers ($p = 0.04$), which means hematocrit in the second half of pregnancy in these people has been more than others.

Table 1. The comparison of average hemoglobin and hematocrit in the first and second half of pregnancy outcome

Pregnancy outcome		Hemoglobin		Hematocrit	
		First half	Second half	First half	Second half
PPROM	Affected by PPROM	12.16 (1.78)	11.15 (1.60)	37.11 (3.63)	35.19 (2.28)
	Not affected by PPROM	12.63 (1.04)	11.93 (1.00)	38.23 (3.06)	36.30 (2.81)
Preeclampsia	Affected by preeclampsia	12.12 (1.36)	11.74 (1.55)	36.95 (3.30)	36.86 (2.78)
	Not affected by preeclampsia	12.62 (1.06)	11.91 (1.01)	38.21 (3.10)	36.25 (2.83)
Delivery type	Vaginal delivery	12.55 (1.09)	11.87 (1.03)	37.96 (3.14)	36.20 (2.77)
	Cesarean section	12.66 (1.05)	11.93 (1.02)	38.34 (3.04)	36.32 (2.84)

Numerical values were represented as mean (standard deviation); PPROM: preterm premature rupture of membrane
It was shown that mean hemoglobin in the second half of the pregnancy in the group with PPROM was significantly less than others.

Discussion

In this study, the average hemoglobin in the second half was significantly lower in the group who later suffered from preterm premature rupture of membranes than other mothers. Ferguson et al. also showed that premature rupture of membranes before 37 weeks was significantly more in women with hemoglobin below 11 g/dl than others. They believed that low levels of hemoglobin may be a sign of a concealed infection.[14] In their study, Zhang et al. also discovered a relationship between low levels of hemoglobin and increase in the risk of preterm premature rupture of membranes later in pregnancy.[15] From the viewpoint of these researchers, low levels of hemoglobin (anemia) early in pregnancy or during pregnancy, which is caused either by previous anemia or the anemia occurred during pregnancy can predispose the mother to infections, hypoxia or oxidative stress and thereby lead to preterm delivery. The proposed explanation for this relationship was the lower socioeconomic and nutritional condition in these mothers.[16] Additionally, our data suggested that hemoglobin in the first half was significantly lower in women who developed preeclampsia. Through the study conducted on 162 pregnant mothers, Karaflahin et al. reported that low level of hemoglobin is associated with increase in the risk of preeclampsia. Thus, it was stressed that family planning and pre-pregnancy assessments is needed to reduce the adverse effects.[17] Patra et al. also concluded that low levels of hemoglobin in the early pregnancy is associated with preeclampsia and eclampsia and declared that low intervals between pregnancies and low nutritional supports lead to low levels of hemoglobin and adverse pregnancy complications, particularly in multiparous women.[18] Although the reason for the relationship of low levels of hemoglobin with complications such as preeclampsia is still completely unknown, factors such as lack of other nutrients in people with low level of hemoglobin,[19] intensification of oxidative stress,[20] endothelial malfunction, mediation of inflammatory responses and insulin function are among the proposed reasons which need further investigations.[21] This can be due to the lower socio-economic status of these women.

In this study, it became clear that the significant inverse relationship between hematocrit in the second half and birth weight and height was overshadowed by gestational age and in fact gestational age is the most important variable associated with hematocrit values. The indices of birth weight, height and head circumference are also influenced by gestational age more than other variables ($p < 0.001$). The significant inverse relationship between the hematocrits in the two halves of pregnancy and gestational age can be noted as one of the other results obtained in this study. Accordingly, by increase in gestational age, hematocrit decreased and physiological dilution of blood became more visible. Through the progress of normal pregnancy, red cell mass will increase 25% and plasma volume will increase 40% which increases uterine placental blood flow through the decrease in blood hematocrit and viscosity as well as peripheral resistance.[8] On the other hand, need for iron is increased during the second half of pregnancy (an average of 6-7 mg per day) which in turn reduces the concentration of the mothers' hemoglobin and hematocrit.[22]

The main reason for the increased hemoglobin and hematocrit levels in the second half of pregnancy in various studies [16,22-24] was blood concentration or in the other words, lack of physiological dilution of blood in the pregnant mothers. Thus, changes in hemoglobin and hematocrit values in the two halves of pregnancy were determined for the subjects through studying the difference between hemoglobin and hematocrit in the second half of pregnancy compared to the first half of pregnancy[16] and the relationship between the obtained variables and pregnancy outcome was analyzed. In this study, the difference between hematocrits in the two halves of pregnancy was significantly correlated with the risk of preeclampsia so that in patients with preeclampsia, hematocrit in the second half reduced less than other mothers. Von Tempelhoff et al. also showed that lack of decrease in hematocrit during the second half of pregnancy compared to the first half was significantly correlated to the risk of preeclampsia.[24] Chang et al. also showed the relationship between hematocrit values above 44 percent in the third trimester and adverse perinatal outcome in women with preeclampsia.[25] In his study, Steer also showed that the hemoglobin levels above 12 g/dL at the late second trimester were associated with three times increase in the risk of preeclampsia.[26] Hematocrit values equal with or greater than 40 percent are because of the increase in the number of red blood cells or more likely, lack of physiological increase in plasma volume.[10] Blood concentration is one of the main symptoms of preeclampsia and is probably caused by generalized vasoconstriction and endothelial dysfunction associated with increased vascular permeability. Depending on the disease severity, blood concentration increases with

preeclampsia, while in women with pregnancy induced hypertension, blood volume is usually normal.[7] It seems that the significant relationship of the difference between hematocrit in the two halves of pregnancy with preeclampsia development was caused by blood concentration in this study.

Using multivariate regression analysis, it was shown that the relationship between gestational age and the difference between hematocrit in the two halves of pregnancy was stronger. Amburgey et al. also suggested that the strong relationship between hemoglobin level and gestational age in women with preeclampsia and less gestational age is probably because of higher blood concentration in these women compared to women with preeclampsia but more gestational age.[16] Generally, according to the results of this study, it can be concluded that gestational age is the main factor associated with the hematocrit values, so that increase in gestational age leads to decrease in hematocrit. However, although the relationship between the two variables was not significant in this study and with this sample size, it seems that hemoglobin also decrease with increase of gestational age. Nevertheless, hematocrit is a parameter with more accuracy.

In conclusion, one of the results obtained in this study was the significant relationship of the difference between hematocrit in the two halves of pregnancy with preeclampsia. Therefore, lack of decrease in hematocrit in the second half in those with preeclampsia or those who are going to show signs and symptoms of preeclampsia within the next weeks, can have clinical application. In addition, the significant relationship between low levels of hemoglobin in the first half of pregnancy and preeclampsia as well as the significant relationship between low levels of hemoglobin in the second half of pregnancy and risk of preterm premature rupture of membranes might be useful to identify the women at risk of these complications and to perform the preventive measures.

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