Effect of Gestational Hypertension on Neonatal Hemoglobin Level

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Abstract- This study aims to determine the effect of gestational hypertension on neonatal hemoglobin levels. This cohort study was performed on 150 pregnant women, 60 of whom had gestational hypertension and 90 were healthy. Participants were selected using sequential and quota non-probability sampling methods, respectively. The data were collected from interviews and examination forms. The newborns' umbilical cords were clamped 30-60 sec after the delivery in both groups. Umbilical cord blood samples were taken to determine neonatal hemoglobin levels and sent to the laboratory immediately. Independent t-test was used to compare the two groups in terms of mean hemoglobin; general linear model with an identical link function was used to compare the two groups in terms of mean hemoglobin, considering the effect of confounding variables. SPSS software version 25 was used for the statistical analysis of the data. The statistical significance level in this study was considered to be 0.05. The mean neonatal hemoglobin level in women with gestational hypertension was significantly higher than that in the healthy group (16.73±1.81 gr/dl vs. 15.56±1.79, P<0.001). This difference remained significant after adjusting for demographic and background variables as well as medical records of the participants (P=0.008). The results revealed the hemoglobin level of newborns of mothers who had gestational hypertension, was higher than newborns of healthy mothers. Therefore, performing proper screening tests and knowledge of the hemoglobin level in these infants routinely helps the healthcare staff to prevent, decide and provide more and more useful services.

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Introduction

Blood pressure disorders during pregnancy are among the important unresolved issues in obstetrics. Gestational hypertension is among the most common disorders, which generally occurs in 12-22% of cases (1) and can cause many fetal and maternal complications including increased fetal and neonatal mortality (2), preterm delivery, low birth weight, intrauterine growth restriction, abruptio placentae, increased rate of cesarean delivery, heart failure, kidney failure and hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome (3). Despite its problematic nature, no specific treatment has yet been found for gestational hypertension and its numerous complications (4).

Special attention has recently been paid to risk factors in order to prevent pregnancy-induced hypertension and its maternal and fetal complications (5). Early prevention of a disease requires a good understanding of its causes. Given that the exact cause of gestational hypertension is unknown, secondary preventive measures have focused on processes such as vasoconstriction, placental development-related disorders, and decreased vascular resistance to hypertensive agents, placental peptide hormones, antioxidants, and genetic factors (6).

Normally, plasma volume increases in the second trimester of pregnancy, and hemoglobin and hematocrit levels decrease in pregnant women. If the increase in plasma volume and subsequent decrease in hemoglobin

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and hematocrit does not occur in women with gestational hypertension, it can be associated with an increase in the risk of maternal and fetal complications (7). Previous studies have shown significant correlation between the maternal hemoglobin level and hemoglobin concentration of the umbilical cord (8,9). Therefore, any increase or decrease in maternal hemoglobin level can directly affect the fetus (10). The change in fetal hematopoiesis results in abnormal hemoglobin level at birth, which can cause irreversible disorders for the person in the future (11). The relationship between neonatal hemoglobin level and gestational hypertension has not yet been determined (12). A few studies have examined hemoglobin concentration in newborns with hypertensive mothers as an appropriate and inexpensive indicator. Moreover, lifestyle, race, and socioeconomic and climatic conditions can all affect the hemoglobin level at birth. Therefore, there should be a clear picture of the hematological status of neonates in each region due to its specific conditions (13-15). To the best of our knowledge, no study has ever been conducted in Iran to investigate neonatal hemoglobin level and its association with gestational hypertension (16). Also, there is a limited number of studies in this field in other countries and the exact hemoglobin level of newborns with hypertensive mothers has never been compared with that of newborns with healthy mothers. Due to the high prevalence of gestational hypertension and its widespread complications as well as the high costs imposed on the individual and society because of its treatment, the present study aims to determine the effect of gestational hypertension on neonatal hemoglobin level.

Materials and Methods

This cohort study was conducted on 150 pregnant women, 60 of whom had gestational hypertension and 90 were healthy. Women with gestational hypertension were selected using sequential non-probability sampling method, i.e., women with gestational hypertension who met the inclusion criteria, were included in the study according to the order of referring to the clinic until the required sample size was obtained. Healthy pregnant women were selected using quota non-probability sampling method. The two groups were matched in terms of maternal gestational week, age, and education level.

According to Kalavakurau Mouna *et al.*,'s study and the following formula, the sample size was calculated as 57 women in the hypertensive group. Finally, 60 women were selected considering the attrition rate. The sample size in the healthy group was considered to be 1.5 times of the sample size in the hypertensive group. Thus, in total, 150 women were included.

$$n = \frac{(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 \ (S_1^2 + S_2^2)}{\mathrm{d}^2} = \frac{(1.96 + 0.84)^2(1.17^2 + 0.65^2)}{0.5^2} \cong 57$$

All 21-week pregnant women referring to the clinic of Asaliyan Hospital were included in the study and followed up until delivery. The newborns' umbilical cords were clamped 30-60 sec after delivery in both groups. Then, umbilical cord blood samples were taken to determine neonatal hemoglobin level and immediately sent to the laboratory. Also, women diagnosed with gestational hypertension were followed up for 12 weeks after delivery to rule out chronic hypertension. Finally, the samples who met all the inclusion criteria remained in the study. The collected data were statistically analyzed. Inclusion criteria were pregnant women who had hypertension (preeclampsia/eclampsia syndrome) since the 21st week of pregnancy. Exclusion criteria were women with risk factors for anemia and polycythemia, folic acid deficiency, vitamin B12 deficiency, iron deficiency, thalassemia, chronic infections, acute blood loss, sideroblastic anemia, kidney failure, bone marrow aplasia, bone marrow fibrosis, intravascular hemolysis, autoimmune disease, hemoglobinopathy, delayed umbilical cord clamping, smoking, diabetes, hyperthyroidism, hypothyroidism, fetomaternal blood transfusion, intrauterine hypoxia, blood toxicity, and placental insufficiency. Also, women with chronic hypertension and those taking medication affecting blood parameters were excluded from the study.

Data collection tools included a demographic questionnaire, observation and examination form, information form related to current pregnancy and medical record, mechanical scale for measuring maternal weight, single-pan scale for measuring newborn's weight, measuring tape, mercury sphygmomanometer and medical earphone.

The validity of observation and examination form as well as information form related to current pregnancy and medical record was determined by content validity index. After reviewing the relevant scientific books and papers, these forms were designed by the research team. The final form was confirmed considering the corrective opinions of 11 faculty members and used to collect the data. The maternal weight was measured using a

mechanical scale (Hadiyeh, Iran). The newborn's weight was measured by a single-pan scale (SECA, Germany). A mercury sphygmomanometer (Teb Abzar, Iran) and non-elastic plastic measuring tape were employed.

The reliability of the observation and examination form as well as information form related to current pregnancy and medical record was determined by inter-rater agreement. For this purpose, these forms were completed regarding 10 participants by the researcher and research assistant separately, but simultaneously. Then, correlation coefficient between the results was calculated and the reliability of the observation and examination form (r=1) and information form related to current pregnancy and medical record (r=0.99, P<0.001) was confirmed.

The reliability of the researcher's and research assistant's performance was obtained in determining maternal blood pressure. The researcher and research assistant determined the blood pressure of 10 pregnant women. Then, correlation between the results was calculated and confirmed with the coefficient of r=0.99 (P<0.001). The reliability of the scale used for measuring maternal weight was determined each time before weighing the healthy mother with the standard weight of 1 kg. The reliability of the scale used for measuring the newborn's weight was determined each time before weighing the newborn of healthy mothers with the standard weight of 500 g. The reliability of measuring tape was assessed using a standard wooden rigid ruler. The reliability of the sphygmomanometer was determined by involving healthy mothers and confirmed by comparing the obtained values with those of another sphygmomanometer at the beginning of and during the study.

The data were described as mean and standard deviation (mean±SD) for the quantitative variables, and frequency and percentage for the qualitative variables. The two groups were compared in terms of mean hemoglobin level using independent t-test. The two groups were compared in terms of mean hemoglobin level using the generalized linear model with identity link function considering the effect of confounding variables. The data were analyzed by SPSS software (version 16.0). The level of significance was considered to be 0.05.

Results

There was a statistically significant difference between the two groups in terms of distribution of maternal weight, infertility duration, gestational age, and number of abortions (P<0.001). However, there was no statistically significant difference between the two groups in terms of maternal age and height and number of pregnancies and deliveries (Table 1).

Table 1. Reproductive characteristics in the hypertensive and healthy groups

Variables	Group				*P**
	Healthy women		Gestational hypertensive women		
	Median	Interquartile range	Median	Interquartile range	
Infertility duration	0.00	0.00	0.00	1.75	<0.001
Gestational age	39.00	2.00	37.00	2.00	<0.001
Number of pregnancies	2.00	2.00	2.00	2.00	0.891
Number of deliveries	1.00	2.00	1.00	2.00	0.267
Number of abortions	0.00	0.00	0.00	1.00	0.006

The two groups were compared in terms of background and clinical variables using Mann-Whitney test (Table 2). There were significant differences between the two groups in terms of maternal educational level (P=0.037) and occupation (P=0.002), husband's educational level (P=0.008) and occupation (P=0.024), household size (P=0.001), place of residence (P=0.007), and history of infertility treatment (P<0.001). There was no statistically significant difference between the two groups in terms of ethnicity, income sufficiency, economic status, history of a specific disease, stillbirth, and regular exercise during pregnancy (P>0.05).

The two groups were compared in terms of background and clinical variables using Fisher's exact test and Chi-square test.

There was a significant direct and linear correlation between neonatal hemoglobin level and age (P=0.021, r=0.189), weight (P=0.002, r=0.246), and number of abortions (P=0.005, r=0.229). However, there was no significant linear correlation between neonatal

hemoglobin level and maternal height, infertility duration, gestational age, number of pregnancies and number of deliveries (P>0.05). Also, there was a direct correlation between neonatal hematocrit level and age (P=0.045, r=0.164), weight (P=0.041, r=0.167), and number of abortions (P=0.001, r=0.273). However, there was no statistically significant correlation between neonatal hemoglobin level and maternal height, infertility duration, gestational age, number of pregnancies, and number of deliveries (Table 3).

Table 2. Demographic and clinical characteristics in the hypertensive and healthy groups

Variables		Group				*P**
		Healthy women		Gestational hypertensive women		
		Frequency	Percentage	Frequency	Percentage	
Maternal educational level	Illiterate / elementary school	21	23.3%	4	6.7%	0.037
	Middle school	17	18.9%	12	20.0%	
	Secondary school	36	40.0%	26	43.3%	
	Academic degree	16	17.8%	18	30.0%	
Maternal occupation	Housewife	85	94.4%	46	76.7%	0.002
	Employed	5	5.6%	14	23.3%	
Husband's educational level	Illiterate / elementary school	22	24.4%	5	8.3%	0.008
	Middle school	14	15.6%	6	10.0%	
	Secondary school	38	42.2%	26	43.3%	
	Academic degree	16	17.8%	23	38.3%	
Husband's occupation	Unemployed	12	13.3%	7	11.7%	0.024
	Worker	29	32.2%	10	16.7%	
	Employee	7	7.8%	15	25.0%	
	Farmer/rancher	13	14.4%	11	18.3%	
	Other	29	32.2%	17	28.3%	
Household size	2-3	28	31.1%	36	60.0%	0.001
	4-5	47	52.2%	22	36.7%	
	6-7	15	16.7%	2	3.3%	
Place of residence	City	41	45.6%	41	68.3%	0.007
	Village	49	54.4%	19	31.7%	

Table 3. Correlation between neonatal hemoglobin and hematocrit levels and other demographic characteristics

Variables	Spearman's correlation coefficient test results	Neonatal hemoglobin	Neonatal hematocrit
Maternal age	Correlation coefficient	0.189	0.164
	*P**	0.021	0.045
Maternal weight	Correlation coefficient	0.246	0.167
	*P**	0.002	0.041
Number of abortions	Correlation coefficient	0.229	0.273
	*P**	0.005	0.001

The correlation between neonatal hemoglobin and hematocrit levels and other background and demographic variables was investigated using Spearman's correlation coefficient test

There was no statistically significant correlation between neonatal hemoglobin and hematocrit levels and maternal educational level and occupation, husband's educational level and occupation, income sufficiency, household size, economic status, ethnicity, stillbirth, regular exercise during pregnancy, place of residence, history of a specific disease, and history of infertility treatment (P>0.05).

Results of the generalized linear model with identical link function showed there was a significant difference between the two groups in terms of mean neonatal hemoglobin level by modulating the effect of confounding variables, i.e., place of residence, history of a specific disease, history of infertility treatment, maternal age and weight, infertility duration, and number of abortions (P=0.008), so that the mean adjusted neonatal hemoglobin levels in hypertensive and healthy groups were about 16.73 and 15.76,

respectively, i.e., this factor in hypertensive group was about 1.17 units more than that in the healthy group. However, results of the generalized linear model with identical link function showed a statistically significant difference between the two groups in terms of mean neonatal hemoglobin level without modulating the effect of the confounding variables (P<0.001).

Results of the generalized linear model with identical link function indicated a significant difference between the two groups in terms of mean neonatal hematocrit level by modulating the effect of the confounding variables, i.e., place of residence, history of a specific disease, maternal age and weight, gestational age, and number of abortions (P=0.042), so that the mean adjusted neonatal hematocrit levels in hypertensive and healthy groups were about 48.09 and 46.00, respectively, i.e., this factor in hypertensive group was about 2.09 units more than that in the healthy group. However, results of the generalized linear model with identical link function demonstrated a statistically significant difference between the two groups in terms of mean neonatal hematocrit level without modulating the effect of the confounding variables (P<0.006) (Table 4).

Table 4. Comparison of neonatal hemoglobin and hematocrit levels in the hypertensive and healthy groups

Variables	Group								*P* 1*	*P* 2*
	Healthy women				Gestational hypertensive women					
	Mean	SD	Median	Interquartile range	Mean	SD	Median	Interquartile range		
Neonatal hemoglobin	15.56	1.79	15.40	2.83	16.73	1.81	16.85	2.68	<0.001	0.008
Neonatal hematocrit	46.00	4.69	46.20	7.15	48.09	4.48	48.35	5.40	0.006	0.042

*P 1 and P 2 were obtained without and with modulating the effect of confounding variables, respectively.

Discussion

The results indicated a significant difference between the two groups in terms of mean neonatal hemoglobin level, so that the mean adjusted neonatal hemoglobin levels in hypertensive and healthy groups were about 16.73±1.81 and 15.56±1.79, respectively, i.e., this factor in hypertensive group was about 1.17 units more than that in the healthy group. This difference remained significant after adjusting demographic and medical variables of the pregnant women.

Mouna *et al*., (17) conducted a study on 120 newborns with hypertensive and healthy mothers (N=60 per group) in India in order to determine changes in blood parameters of newborns, the mothers of whom had gestational hypertension. The mean cell volume (MCV), hemoglobin level, red blood cell count, reticulocyte count, and nucleated red blood cell (NRBC) were significantly higher. Also, total white blood cell, neutrophil, lymphocyte, and platelet counts were significantly lower, which was consistent with the results of the present study.

In our work, there was a significant difference between the two groups in terms of mean neonatal hematocrit level, so that the mean adjusted neonatal hematocrit levels in hypertensive and healthy groups were about 48.09±4.48 and 46.00±4.70, respectively, i.e., this factor in the hypertensive group was about 2.09 units more than that in the healthy group. Okoye *et al*., (18) investigated the correlation between hematocrit level and Apgar scores of newborns with hypertensive mothers in Nigeria. Also, a comparison was made between the incidence of polycythemia in newborns with hypertensive and healthy mothers. The result showed hematocrit level was positively correlated with Apgar score. The incidence of polycythemia in the newborns with hypertensive mothers was greater than that among the newborns with healthy mothers. Apgar score was affected by hematocrit which itself was influenced by gestational hypertension. However, in our study, Apgar score was not evaluated as a variable.

In line with results of our research, Al-bahadily *et al*., (19) examined the effect of gestational hypertension on neonatal blood parameters in Iraq. For this purpose, 200 newborns with hypertensive and healthy mothers were selected (N=100 per group) and their Apgar scores, birth weight, gestational age, and blood parameters were assessed. The results showed a significant difference between the two groups in terms of Apgar score, birth weight, gestational age, hemoglobin level, white blood cell count, and platelets, which was affected by gestational hypertension.

Farooqui *et al*., (20) evaluated the effect of preeclampsia on neonatal red blood cell parameters in India. The results revealed preeclampsia increased red blood cells, reticulocytes, and reticulocyte production

index (RPI). Consistent with our research, preeclampsia reduced neonatal hemoglobin and hematocrit levels, which was probably due to the differences in the studied samples or demographic characteristics. Moreover, lifestyle, race, as well as socioeconomic and climatic conditions could affect the hemoglobin level at birth.

Eman *et al*., (21) examined umbilical cord blood samples of newborns with hypertensive and healthy mothers, compared their hematological profiles, and evaluated short-term clinical outcomes in newborns in India. Both groups were followed up for clinical outcomes during the period they were hospitalized. The results showed gestational hypertension could be associated with leukopenia, neutropenia, thrombocytopenia, and increased NRBC. Also, gestational hypertension could increase the relative risk of sepsis and neonatal mortality. However, this correlation was not statistically significant. It was found that gestational hypertension could increase hemoglobin and hematocrit levels, which was in line with our results. Okoy *et al*., (22) investigated the effect of gestational hypertension on neonatal hemogram and compared the incidence of neonatal polycythemia, neutropenia, and thrombocytopenia in Nigeria. The results revealed the mean hematocrit level in the case group was significantly higher than the control group, while neutrophils and platelets of the newborns in the case group were significantly lower than the control group. The incidence of polycythemia, neutropenia, and thrombocytopenia was 8%, 15%, and 38% in the case group and 0%, 2%, and 8% in the control group, respectively. Results of various studies have demonstrated gestational hypertension can affect neonatal blood parameters and this finding was proven in the above-mentioned research.

One of the limitations of this study was the lack of necessary tests to fully investigate blood parameters, which considering that other blood parameters such as platelets are also very affected in the health of newborns, it is suggested that blood parameters be fully investigated in future studies; Also, one of the other limitations was the small number of samples of mothers suffering from pregnancy-related hypertension in Asali Hospital, which suggests that samples should be collected from other medical centers in future studies.

The results indicated hemoglobin level in newborns with hypertensive mothers was significantly higher than that in newborns with healthy mothers; this difference remained significant after adjusting demographic, background variables, and medical records of the participants. Therefore, due to the high prevalence of gestational hypertension and its adverse effects in newborns, being aware of neonatal hemoglobin level routinely can help health care providers take preventive measures, make decisions, and provide services that are more useful.

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