

Maternal Anemia and Prenatal Complications

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ABSTRACT: Severe anemia in mothers is associated with low birth weight, premature delivery, and fetal death. This cross-sectional study aimed to determine the relationship between the hemoglobin level and hematocrit of mothers and prenatal complications. Subjects consisted of 1100 pregnant that had referred to Bandar Abbas' Shariati hospital in 2007 that had a single, viable fetus with cephalic presentation without diabetes mellitus, hydramnios, hemorrhage during pregnancy or delivery, apparent congenital fetal anomalies, pre-eclampsia or eclampsia. Blood tests were performed to measure hemoglobin and hematocrit. Information regarding the mother and newborn and its perinatal complication was gathered via a questionnaire. The effects of hemoglobin level and hematocrit on perinatal complications were estimated using descriptive statistical methods and multiple logistic regressions with a 95% confidence interval and a precision of 2%. The prevalence of low birth weight and prematurity in mothers with hemoglobin levels less than 10.5 g/dl was 8% and 8%, respectively which was higher than those of mothers with hemoglobin levels between 10.5-13 g/dl. The risk of the need for intensive care unit admission in subjects with hematocrit above 40% was 2.34 times more than that of subjects with hematocrit between 34 and 40%. Low hemoglobin level in pregnant mothers increases the risk of low birth weight, premature delivery and low Apgar score in the fetus and a high percentage of hematocrit is associated with an increased risk of intensive care unit admission. Therefore this should be taken into consideration in perinatal care.

Keywords: Anemia, Pregnancy, Low Birth Weight, Premature Birth, Intensive Care Unit, Neonatal

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INTRODUCTION

There are a lot of maternal factors which effect on the pregnancy prognosis. One of these factors is maternal anemia that is detected with decrease in hemoglobin (HbC), red blood cell count (RBC), packed-cell volume (PCV) (Pei et al., 2011). The estimate of WHO about anemia in pregnant women of developing country is an average of 56%, but in developed countries anemia diagnosed in 18% of pregnancies (Laflamme, 2010) and in a nutritional study shows that worldwide prevalence of anemia in pregnancy was 38% (Haider et al., 2013). According to the WHO database, 20.8% of pregnant women in Russia were anemic (Chumak Elena et al., 2010). In a study it was estimated that 87% of the Indian pregnant women were anemic (Kumar et al., 2013).

Most studies shows, the adverse pregnancy outcome in anemic pregnant women. Few studies shows adverse pregnancy outcome with increased level of hemoglobin (Kumar et al., 2013). Some studies showed no association between Hb level and adverse pregnancy outcome (Ren et al., 2007). The complications of maternal anemia including an increased risk of low birth weight, premature delivery, Small for Gestational Age, fetal growth restriction, and still birth are shown in previous studies (Kumar et al., 2013; Levy et al., 2005). A study shows that Anemia is responsible for 15% to 20% of maternal mortality (Patra et al., 2005).

Risk of preterm birth weight and low birth weight in anemic women were, 2.2 and 3.92 times higher than in

non-anemic women (Yousaf et al., 2011). The result of a systematic review showed a relationship between moderate to severe anemia in mother and small for gestational age in new born (Kozuki et al., 2012). Hb level is lower in the middle of pregnancy. Maternal anemia in the middle and late pregnancy is associated with premature infant (12-Cunningham et al, 2010; Garshasbi and Fallah, 2006). These neonates are more vulnerable compared to those with normal birth weight and are susceptible to many health problems (Garshasbi et al., 2006). A study conducted by Wang et al. (2007) shows that severe anemia and high hemoglobin level increased the risk of preterm deliveries and low birth weight (Wang et al., 2007). A high Hb concentration causes an increase in Hct and serum ferritin level in late pregnancy. All of these factors are associated with the risk of premature infants (Malhotra M et al., 2002). On the other hand another study showed that high hemoglobin lowered the risk of premature rupture of membrane (Gonzales et al., 2012). A study in Iran shows no significant association between maternal hemoglobin concentration and birth weight in first and third trimester (Salimy et al., 2012).

Considering the controversial results of the aforementioned studies regarding the effect of mother's Hb level and Hct on perinatal complications in different trimesters, the aim of this study is to determine the relationship between maternal Hb level and Hct and perinatal complications (birth weight less than 2500 gram, prematurity, infant's Apgar score, delivery modality and infant's need for ICU and admission).

MATERIAL AND METHODS

In this study, the subjects consisted of 1100 non-smoking mothers with no previous history of drug abuse referring to Bandar Abbas' Shariati hospital of Iran within 6 months – from September 2007 to March 2008 – who had a single, viable, cephalically-presented fetus without hydramnios, diabetes mellitus, and severe hemorrhage during pregnancy, apparent congenital fetal anomalies, pre-eclampsia and eclampsia. Blood tests were carried out on mothers during admission to measure Hb levels and Hct. Information regarding the mother's age, education level, job, nationality, place of residence, number of pregnancies, deliveries, number of hospital cares during pregnancies, use of iron complements and deliveries' modality were gathered via a questionnaire through an interview. Also, the newborn's birth weight (using special scales in infants' ward), it's Apgar score in the 1st and the 5th minute of life and its need for admission were registered. In addition, fetal age was estimated using mother's LMP or her sonographic images.

The subjects were classified into three groups based on their Hb levels: mothers with Hb levels below 10.5 g/dl, between 10.5 g/dl and 13 g/dl and higher than 13 g/dl. They were also categorized into three groups based on their Hct: subjects with Hct below 34%, between 34% and 40% and above 40%. The main independent variables in this study were Hb level and Hct. The risk ratio of prevalence of perinatal complications in mothers with Hb levels less than 10.5 g/dl or more than 13 g/dl was estimated compared to that in those with Hb levels between 10.5g/dl and 13 g/dl. Also, the risk ratio of prevalence of perinatal complications in mothers with Hct less than 34% or above 40% was estimated compared to that in those with Hct between 34% and 40%, all using descriptive statistics and logistic regression method. After that, the adjusted and unadjusted odds ratio of the effect of both independent

variables (Hb level and Hct) was estimated with a 95% confidence interval after eliminating the influence of maternal age, education level, number of pregnancies, number of deliveries, place of residence and number of perinatal care events.

RESULTS

The mean age of the mothers ($\bar{x} \pm$ standard deviation) in this study was 25.5 ± 5.7 years. As for educational level, 131 subjects (11.9%) were illiterate. The place of residence of 602 subjects (54.7%) was in urban areas. As for job status, the majority i.e. 1061 (96.5%) subjects were housewives. The nationality of 1071 subjects (97.4%) was Iranian. Thirty subjects (2.7%) were visited less than 3 times, and 885 (80.5%) were visited more than 6 times. Eight-hundred twelve subjects (73.8%) used iron complements during pregnancy. The majority of subjects i.e. 964 (87.6%) had NVD. Seventy-one infants (6.5%) had a birth weight less than 2500 gr. Out of 1100 born infants, 1069 (97.2%) did not need to be admitted in critical care unit. As shown in table 1, 188 subjects (17.1%) had Hb levels less than 10.5. The prevalence of perinatal complications (birth weight less than 2500 gram and premature newborn) was 8% and 8%, respectively, in mothers with Hb levels less than 10.5 g/dl, which was greater than the prevalence of such complications in those with Hb levels between 10.5 and 13 g/dl.. In addition, the rate of the need for admission in mothers with Hb levels less than 10.5 g/dl and greater than 13 g/dl was 3.7% and 3.6%, respectively which was higher compared to the group with Hb levels between 10.5 and 13 g/dl (2.2% of patients). the rate of Apgar scores less than 7 in the 5th minute of life in the group with lower Hb levels was 3 times than in those with Hb levels between 10.5 and 13 g/dl.

Table 1. Distribution of maternal hemoglobin level (frequency and percentage) and the prevalence of infant complications

			5 th Minute Apgar Score Less Than 7	Need for Admission	Infant Prematurity	Low Birth Weight	1 st Minute Apgar Score Less Than 7	Type of Delivery	Total
Hemoglobin	<10.5	Frequency	5	7	15	15	14	31	188
		Percentage	2.7%	3.7%	8.0%	8.0%	7.4%	23.5%	17.1%
	>13	Frequency	3	8	11	16	14	21	691
		Percentage	1.4%	3.6%	5.0%	7.2%	6.3%	15.9%	62.8%
	10.5-13	Frequency	6	16	46	40	46	21	221
		Percentage	0.9%	2.3%	6.7%	5.8%	6.7%	15.9%	20.1%
Total		Frequency	14	14	31	72	74	132	1100
		Percentage	1.3%	1.3%	2.8%	6.5%	6.7%	100.0%	100.0%

Table 2. Distribution of maternal hematocrite level (frequency and percentage) and the prevalence of infant complications.

			5 th Minute Apgar Score Less Than 7	Need For Admission	Infant Prematurity	1 st Minute Apgar Score Less Than 7	Low Birth Weight	Type of Delivery	Total
Hematocrite	<34	Frequency	5	8	20	19	18	46	283
		Percentage	1.80%	2.80%	7.10%	6.70%	6.40%	34.80%	25.70%
	>=40	Frequency	3	8	7	10	12	16	662
		Percentage	1.90%	5.20%	4.50%	6.50%	7.70%	12.10%	60.20%
	34-39.9	Frequency	6	15	45	45	41	70	155
		Percentage	0.90%	2.30%	6.80%	6.80%	6.20%	53.00%	14.10%
Total		Frequency	14	31	31	74	72	132	1100
		Percentage	1.30%	2.80%	2.80%	6.70%	6.50%	100.00%	100.00%

Table 3. The unadjusted and adjusted odds ratio of the effects of maternal hemoglobin and hematocrite levels on the occurrence of infant complications

Independent variables	Low birth weight		Prematurity		Need for critical care		1 st minute Apgar score less than 7		5 th minute Apgar score less than 7		Type of delivery	
	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)	(CI 95%)
Hematocrite<34	0.944	1.029	0.944	1.043	0.98	1.255	0.793	0.987	1.199	1.966	0.534	0.603
	(0.508 - 1.753)	(0.580-1.524)	(0.566-1.779)	(0.604-1.8)	(0.378-2.538)	(0.526-2.994)	(0.433-1.453)	(0.566-1.719)	(0.571-8.474)	(0.595-6.497)	(0.83-0.343)	(0.90-0.4.3)
34-40 (ref)	1	1	1	1	1	1	1	1	1	1	1	1
>40	1.536	1.271	0.64	0.648	3.02*	2.347	1.09	0.946	1.187	2.158	0.868	1.029
	(0.762 - 3.1)	(0.651-2.480)	(0.272-1.502)	(0.287-1.467)	(1.186-7.693)	(0.977-5.640)	(0.519-2.290)	(0.466-1.921)	(0.373-13.77)	(0.534-8.725)	(0.475-1.585)	(1.58-1.82)
Hemoglobin <10.5	1.271	1.411	1.121	1.216	1.275	1.632	1.163	1.128	4.194*	3.119*	0.551	0.652
	(0.648 - 2.494)	(0.762-2.614)	(0.586-2.147)	(0.663-2.230)	(0.504-0.750)	(0.661-4.026)	(0.474-1.844)	(0.606-2.1)	(1.074-16.377)	(0.941-10.335)	(0.334-0.908)	(0.415-1.02)
10.5-13 (ref)	1	1	1	1	1	1	1	1	1	1	1	1
>13	1.503	1.27	0.767	0.734	2.086	1.585	1.163	0.948	1.838	1.571	1.249	0.551
	(0.801 - 2.821)	(0.697-2.316)	(0.381-1.546)	(0.374-1.44)	(0.835-5.206)	(0.669-3.754)	(0.474-1.8)	(0.511-1.760)	(0.429-7.879)	(0.390-6.335)	(0.753-2.07)	(0.324-0.908)

Table 2 shows that the prevalence of low birth weight complications in the groups with Hct less than 34% and more than 40% was 6.4% and 7.7%, respectively, which was greater than that of the group with Hct between 34-40% (6.2%). The prevalence of prematurity in the group with Hct less than 34% was 7.1% which was greater than that in the group with Hct between 34-40% (6.8%). But the rate of prematurity did not show any increase in the group with Hct more than 40% (4.5%). The need for admission of the newborn showed a higher increase in the group with Hct greater than 40% (5.2%) compared to that of the group with Hct between 34-40% (2.2%). The rate of Apgar scores less than 7 in the 1st and the 5th minute after delivery was 6.7% and 1.8%, respectively, in the group with Hct less than 34% which was higher compared to that in the group with Hct between 34-40% (6.8% and 0.9%, respectively).

According to Table 3, the adjusted odds ratio of the effect of Hb levels less than 10.5 g/dl on the risk of occurrence of low birth weight, prematurity and the need for admission for critical cares was 1.41 times (CI 95%: 0.76-2.61), 1.21 times (CI 95%: 0.62-2.33) and 1.62 times (CI 95%: 0.66-4.02) that of those with Hb levels between

10.5-13 g/dl, and the adjusted odds ratio of Apgar scores less than 7 was 3.11 times greater (CI 95%: 0.94-10.32) in the group with Hb levels less than 10 g/dl compared to those with Hb levels between 10.5-13 g/dl which has a significant effect on this complication. As shown in table 3, the adjusted odds ratio of the effect of Hct less than 34% on occurrence of low birth weight, prematurity and the need for admission for critical care was 1.02 (CI 95%: 0.58-1.52), 1.04 (CI 95%: 0.60-1.8) and 1.25 times (CI 95%: 0.52-2.99) more than that of the group with Hct between 34-40%, respectively. Also, the unadjusted odds ratio of the effect of Hct more than 40% on the need for admission for critical care was 3.20 (CI 95%: 1.18-7.969) meaning that the risk ratio in this group is 3 times more than that in the group with Hct between 34-40% which has a significant effect on this perinatal complication.

According to the results shown in Table 4, the rate of cesarean section in the group with Hct less than 34% and Hb level less than 10.5 g/dl was 34.8% and 23%, respectively which was higher compared to the groups with greater levels of Hct and Hb.

Table 4.Frequency and percentage of the type of delivery by maternal hemoglobin and hematocrite

Maternal Hemoglobin Level			NVD	Cesarean Section	Vantos	Total
Hemoglobin	<10.5	Frequency	154	31	3	188
		Percentage	16%	23%	0.75%	17.10%
	10.5-13	Frequency	610	21	1	691
		Percentage	63.30%	15.90%	0.25%	62.80%
	>13	Frequency	200	21	0	221
		Percentage	20.70%	15.90%	0%	20.10%
Total		Frequency	964	132	4	1100
		Percentage	100%	100%	100%	100%
Hematocrite	<34%	Frequency	234	46	3	283
		Percentage	24.30%	34.80%	0.75%	25.70%
	34-40%	Frequency	591	70	1	662
		Percentage	61.30%	53%	0.25%	60.20%
	>40%	Frequency	139	16	0	155
		Percentage	14.40%	12.10%	0%	14.10%
Total		Frequency	964	132	4	1100
		Percentage	100%	100%	100%	100%

DISCUSSION

The results of this study showed that birth weights less than 2500 gram and prematurity rates were higher in infants whose mothers had Hb level less than 10.5 which is similar to the findings of Lone et al. in Pakistan in 2004. Also, in a study by Siegari-Riz et al. [1998] in the United States, anemia in the 2nd and 3rd trimester was associated with premature delivery. It is noted in this study that anemia was present in 9% of pregnant women leading to a

possible premature delivery in spite of using iron complements.

In the present study, the rate of prematurity in infants whose mothers had Hct levels less than 34% had an increase almost similar to that in those with mothers with Hb levels less than 10.5 g/dl; whereas Hct levels more than 40% and Hb levels greater than 13.5 g/dl were not associated with the risk of premature newborn. These findings were similar to those in the study by Garshasbi et al in Iran [2006]. Also in a study by Bondivik et al in Nepal [2001] the risk of premature delivery and premature

infants in mothers with Hct levels less than 38% was 2 times that in those with Hct levels between 41-44%.

The rate of low birth weights (LBW) in mothers with Hct levels more than 40% showed an increase similar to that in mothers with Hb levels less than 10.5. School et al. (2002) explained in a review study in the United States that a high concentration of Hct was associated with an increased risk of LBW .whereas Ramezan-ali et al [2004] showed, on the contrary to our study, that there is a significant relationship between the low Hct level and the mean infant weight at the time of delivery.

The risk of an Apgar score less than 7 in infants whose mothers had an Hb level less than 10.5 g/dl showed an increase ($p < 0.05$) which is similar to the results of the study by Lone et al in Pakistan [2004] who had concluded that the rate of Apgar scores less than 5 in the 1st minute of life and the risk of fetal mortality in anemic mothers were 3.7 times more than that in the normal population. The unadjusted odds ratio of the effect of Hct more than 40% on the need for admission for critical cares in infants showed a significant 3-fold increase ($p < 0.05$) which is possibly due to the increase of the LBW rate in this group and the more vulnerable status of its subjects; it could also be because the intervals between deliveries and the number of prenatal cares and the type of delivery had a significant effect on the need-for-admission variable ($p < 0.05$)

Therefore, considering various studies with controversial results regarding the influence of maternal Hb and Hct level on the outcome of pregnancy, it is suggested that studies be carried out in this field in different trimesters of pregnancy. In addition, the rate cesarean sections in mothers with low levels of Hb and Hct showed an increase which is similar to the results of the study by Bondivik et al. (2001) who showed that pregnancy in women with low Hct levels in the 1st and 3rd trimester is associated with cesarean section ($p < 0.001$). Malhotra et al. (2002) showed that the more severe the mother's anemia is, the more the cesarean section rate increases.

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