

ORIGINAL ARTICLE

Hemoglobin Evaluation in Hypertensive Disorders of Pregnancy

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ABSTRACT

Objective: To evaluate the maternal hemoglobin (Hb) concentration and its levels in hypertensive pregnant patients during the third trimester of gestation.

Methods: A prospective cross-sectional study was conducted in an Obstetrics and Gynecology Department of Teaching Hospital affiliated to the University of Lahore from November 2017 to June 2018. All pregnant women aged 18-40 years having third trimester of gestation, who came for antenatal check up or admitted to hospital were consecutively included. The demographic characteristics of pregnant women were documented and Hb concentration was assayed in the hematology laboratory and evaluated in pregnant females with hypertension (Hypertensive pregnant group) and healthy normotensive pregnant women. Hypertensive pregnant group were further categorized as pregnancy induced hypertensive (PIH), pre-eclampsia, and eclampsia.

Results: Of 78 pregnant women (62 hypertensive and 16 normotensive), the median age was 25 (23–29) years. Of 62 hypertensive women, PIH was observed in 33 (42.3%) women, pre-eclampsia in 17 (21.8%), and eclampsia in 12 (15.4%). The median Hb level was observed in 11.5 (10-12) g/dL. The median Hb level in normotensive pregnant women was significantly higher as compared to hypertensive pregnant women, i.e., 11.9 (11.6-12.0) vs. 11.0 (9.5-12.0) respectively (p-value 0.006). Furthermore, among hypertensive women, the median Hb level was insignificantly higher in eclamptic women [11.5 (11.1-12.0)] as compared to PIH [10.7 (9.4-12.2)] and pre-eclamptic women [9.9 (9.5-11.7)] (p-value 0.079).

Conclusion: In the present study, the evaluation of Hb shows a statistically significant deterioration in Hb levels among hypertensive pregnant patients as compared to normotensive pregnant women.

Keywords: Hemoglobin, Eclampsia, Pre-eclampsia, Third trimester.

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INTRODUCTION

Hypertensive disorders especially pre-eclampsia is one of the most important complication of gestation. About five to ten percent of all the pregnancies are complicated by hypertensive disorders that leads to maternal mortality and morbidities.¹ The onset of these pregnancy related hypertensive disorders usually occurs at or after 20th week of gestation. The primary hypertensive disorder has only raised blood pressure that is without proteinuria, known as pregnancy induced hypertension (PIH); or along with proteinuria and multiorgan dysfunction mentioned as pre-eclampsia; and if hypertension is come with seizures it is termed as eclampsia.²

Although, the etiology of pregnancy associated hypertensive disorders has remained unsolved, the possibility of imbalance in angiogenic factors and endothelial dysfunction has been documented.^{3,4}

Anemic pregnancy is related to a harmful impact on mother as well as on developing fetus. So, nearly in all

the developing and many developed countries, anemic pregnancies are the most important public health issue. Studies reported that significant anemia in pregnancy occurs with a prevalence ranging between 2-26%, depending upon the study population. The cut off value of hemoglobin (Hb) for anemia is less than 11.0 g/dl.^{5,6} It is well known that physiologically, Hb concentration falls during gestation. This is because expansion of plasma volume as a mechanism to improve arterial uterine flow to the placenta.^{7,8} In pregnancy, anemia is the most important medical disorder and has different etiology, incidence, and levels of severity in various populations.⁹ Anemic pregnancy has higher maternal mortality and morbidity that results in adverse perinatal outcomes.¹⁰

In Pakistan, a high incidence of obstetric complications has been observed with anemia and gestational hypertension leading to a high maternal mortality¹¹ and there are insufficient information and conflicting literature regarding Hb estimation accompanying hypertensive disorders of pregnancy. So, the present

study was undertaken to evaluate the Hb levels in pregnancy associated hypertensive disorders.

METHODS

The study was conducted in the Institute of Molecular Biology and Biotechnology, Obstetrics and Gynecology Department of UOL teaching hospital affiliated to The University of Lahore from November 2017 to June 2018. Ethical approval was obtained from the university prior conducting the study (IRB # IMBB/UOL/18/110). Moreover, informed consent was also obtained from all study participants.

Patients were included from hospital admission and outdoor patient department. A total of 78 pregnant women, aged 18-40 years having third trimester of gestation, who came for antenatal check up or admitted to hospital were enrolled in the study. Evaluation of gestational age was done by last menstrual period, and further evaluated by early pelvic assessment, and verified by 1st trimester or early 2nd trimester pelvic ultrasound.

Hypertensive pregnant that had history of hypertension not associated with pregnancy, chronic hypertension, cardiovascular diseases, thyroid disorders, kidney disorders, diabetes mellitus, any other medical disorders that may be threatening to the fetus or the mother and patient with prior history of treatment/ medication that might influence the Hb levels were excluded from the research.

Out of 78 pregnant women, 62 were diagnosed with pregnancy related hypertensive disorder. These hypertensive pregnant women were presented with raised systolic/diastolic blood pressure equal and above of 140/90 mmHg at 28th weeks of gestation or above on two separate occasion at least at a difference of 6 hours.¹¹ The hypertensive pregnant patients were further categorized into PIH, pre-eclamptic, and eclamptic. According to the American College of Obstetricians and Gynaecologists (ACOG), the non-proteinuric hypertensive pregnant were grouped as PIH and those with blood pressure that is equal to and more than 140/90mmHg and proteinuria equal to and above 300mg/24 h or with a dipstick value of +1 and more at 20th week of gestations were categorized in pre-eclamptic. While women with blood pressure \geq 140/90 mmHg, with or without proteinuria and convulsions were grouped as eclamptic.¹¹ Moreover, 16 pregnant females were normotensive, i.e., normal blood pressure.

Patients' history was taken with detailed medical examination. The related data were documented on

questionnaire, including age, obstetric history, parity, gravidity, weight, socioeconomic status, medication and previous history of hypertension and other medical issues. A venous blood sample was taken in a 3.5 ml evacuated tube containing Ethylenediaminetetraacetic acid (EDTA) and then analyzed for Hb levels by using Sysmex KX21 hematology analyzer.

Data were entered and analysed on SPSS version 20. Median and inter quartile range was calculated for age, gestational weeks, blood pressure, and Hb level. Frequencies and percentages were calculated for categorical variables like hypertensive disorder, gravida, and abortion. Inferential statistics were explored using Mann-Whitney U test and Kruskal-Wallis test for median difference of Hb level with respect to baseline and clinical characteristics based on hypertensive disorders. Chi-square test for comparison of Hb level with hypertensive disorder. p-value \leq 0.05 was taken as significant.

RESULTS

Of total 78 pregnant women (62 hypertensive and 16 normotensive), the overall median age of the pregnant women was 25 (23–29) years. The median gestational age, systolic blood pressure and diastolic blood pressure was 34 (31-36) weeks, 140 (130-150) mmHg and 90 (90-100) mmHg respectively. The history of abortion was observed in 14 (17.9%) women.

Among 62 hypertensive women, with PIH was observed in 33 (42.3%) women, pre-eclampsia in 17 (21.8%), and eclampsia in 12 (15.4%) women.

The median HB level was observed in 11.5 (10-12) g/dL. The median Hb level in normotensive pregnant women was significantly higher as compared to hypertensive pregnant women, i.e., 11.9 (11.6-12.0) vs. 11.0 (9.5-12.0) respectively (p-value 0.006). Furthermore, among hypertensive women, the median Hb level was insignificantly higher in eclamptic women [11.5 (11.1-12.0)] as compared to PIH [10.7 (9.4-12.2)] and pre-eclamptic women [9.9(9.5-11.7)] (p-value 0.079). (Table 1) The median difference of Hb level with baseline and clinical characteristics showed that in normotensive patients, a significant median difference of Hb was observed with gravida (p-value 0.027). In eclamptic women, a significant difference of Hb was observed with gravida (p-value 0.005) and parity (p-value 0.031). While in pre-eclamptic women, a significant difference of Hb was observed with parity (p-value 0.050). (Table 2) There were 31 (39.7%) women with anemia (Hb level <11g/dL). In normotensive women, none of the patients was anemic. Whereas among 62 hypertensive women,

Table 1: Median difference of hemoglobin level among patients with and without hypertensive disorder (n=78)

	Hemoglobin level (g/dL)	
	median (IQR)	p-value
Hypertensive status		
Normotensive	11.9 (11.6-12.0)	0.006*~
Hypertensive	11.0 (9.5-12.0)	
With Hypertensive		
Eclamptic	11.5 (11.1-12.0)	0.079^
Pre-eclamptic	10.7 (9.4-12.2)	
PIH	9.9 (9.5-11.7)	

~Mann-Whitney U Test and ^Kruskal Wallis Test applied, PIH: Pregnancy-Induced Hypertension, *p-value ≤0.05

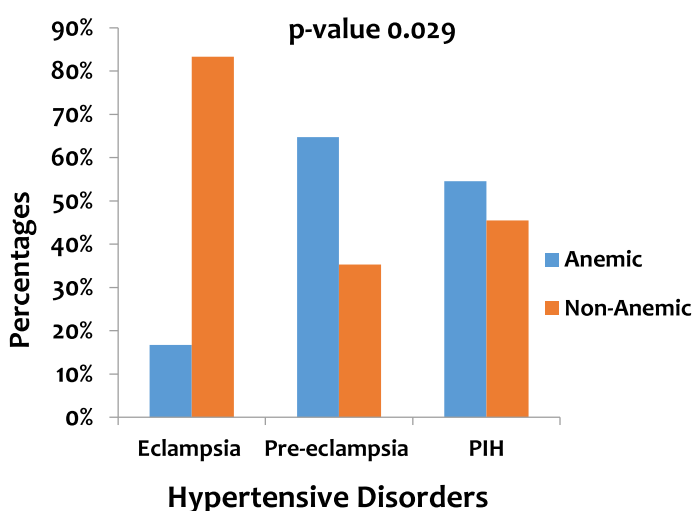


Figure 1: Comparison of hemoglobin level with hypertensive disorder

anemia was significantly higher in pre-eclamptic women 11 (64.7%) as compared to PIH 18 (54.5%) and eclamptic 2 (16.7%) (p-value 0.029). (Figure 1)

DISCUSSION

The present study demonstrated that a decrease in Hb concentrations in the third trimester was associated with the hypertensive disorders of pregnancy. The results of our study interpreted statistically significant relation between anemia and hypertensive disorders of pregnancy. It is reported that anemic in pregnancy is a major maternal and fetal health issue. Anemic pregnancies are five times at the threat of complications particularly pre-eclampsia and even the maternal death.¹² According to a WHO report, fifty two percent of the pregnant females are anemic in the developing countries. Anemia is also common in Pakistan and it affects twenty nine to fifty percent of

pregnant women.¹³ Physiological hemodilution during pregnancy occurs to build a low viscosity intravascular circulation that permits optimum red cell movement in the low velocity placental circulatory environment.¹⁴ This continuous hemodilution and anemia till the third trimester could be credited to a shortage in micronutrients and antioxidants because of poor nutritional and low socio-economic status in pregnant hypertensive disorders.¹⁵

The current study enrolled including hypertensive and normotensive women. Among hypertensive women, PIH was observed in four two percent women, pre-eclampsia in twenty two percent, and eclampsia in fifteen percent women. Pregnant women included in the study had a median age of twenty-five years. The young age was probably because of the fact that in our population early marriages are more common. Mtali et al, and Gupta et al reported a mean age of twenty-nine years in their study^{16,17} whereas Enaruna et al showed thirty years (range nineteen to forty-one) in similar study associated with increased risk of hypertensive disorders especially pre-eclampsia.¹⁸ In our study the median gestational age was thirty-four weeks which was same in both the comparison groups. The systolic and diastolic blood pressure was one forty mmHg and ninety mmHg respectively. Literature also reveals similar demographic data including age, gestational age, and blood pressure.^{16,17} The occurrence of abortion was observed in eighteen percent women only. So, mostly there was no significant history of miscarriages in our study population.

In terms of gravida and parity, our study elaborated significant median difference of Hb with gravida in normotensive patients. Among the hypertensive pregnant, eclamptic women had a significant difference of Hb with gravida and parity. While in pre-eclamptic women, a significant difference of Hb was observed

Table 2: Median difference of hemoglobin level with respect to baseline and clinical characteristics stratified based on hypertensive disorders (n=78)

Variables	Normotensive		Eclampsia		Pre-eclampsia		PIH	
	median (IQR)	p-value	median (IQR)	p-value	median (IQR)	p-value	median (IQR)	p-value
Age, years								
≤25	11.9 (11.6-12.0)	0.195 [~]	9.8 (9.1-11.8)	0.850 [~]	11.5 (11.1-12.0)	>0.999 [~]	10.8 (10.0-11.8)	0.729 [~]
>25	11.6 (11.4-11.9)		9.9 (9.5-11.7)		11.5 (11.0-12.0)		10.7 (9.2-12.4)	
Gestational age, weeks								
≤34	11.9 (11.5-12.0)	0.809 [~]	11.5 (11.1-12.0)	>0.999 [~]	9.5 (7.8-12.0)	0.184 [~]	10.1 (9.2-11.1)	0.113 [~]
>34	11.8 (8.8-11.8)		11.5 (8.6-11.4)		10.1 (9.6-11.7)		11.4 (9.5-12.5)	
Gravida								
Primigravida	12 (11.9-12.2)	0.027 ^{*~}	11.5 (11.1-12.0)	0.005 ^{*~}	9.5 (9.2-9.8)	0.167 [~]	10.3 (10.1-12.8)	0.688 [~]
Multigravida	11.7 (11.4-11.9)		11.5 (8.6-11.4)		10.8 (9.5-11.9)		10.8 (9.3-12.1)	
Parity								
Nulliparous	12 (11.6-12.1)		11.3 (11.0-11.5)		9.5 (9.3-9.7)		10.3 (10.1-12.8)	
Primiparous	11.9 (11.7-12.0)	0.183 [^]	12.7 (9.0-12.8)	0.031 ^{*^}	11.5 (7.6-12.1)	0.050 ^{*^}	10.0 9.3-11.5	0.979 [^]
Multiparous	11.6 (11.3-11.9)		12.0 (9.0-12.3)		10.3 (9.7-11.8)		11.5 (9.2-12.5)	
Abortion								
Yes	11.6 (11.4-12.0)	0.338 [~]	-	0.102 [~]	11.7 (9.5-12.0)	0.341 [~]	11.5 (9.3-12.5)	0.775 [~]
No	11.9 (11.6-12.0)		11.5 (11.1-12.0)		9.7 (9.3-11.5)		10.6 (9.4-12.0)	

[~]Mann-Whitney U Test and [^]Kruskal Wallis Test applied, PIH: Pregnancy-Induced Hypertension, *p-value ≤0.05

with parity. Median IQR is low in nulliparous as compared to primi and multiparous. These findings are consistent with previous studies done in other countries that also showed that the maternal age, gravida, and parity was lowest in hypertensive disorders of pregnancy.¹⁹ In another study from Oman Hb levels were lower in hypertensive pregnant women with increasing parity which proves that anemia become sever with increasing parity.²⁰ A study from Turkey in 2017 interpreted that prevalence of anemia was high in multiparous and grandparous pregnant females.²¹ These results are relatable to our results in terms of gravida and parity especially in eclamptic and pre-eclamptic pregnant females.

The current study showed significantly high median Hb levels in normotensive pregnant as compared to hypertensive pregnant women. Mtali *et al* mentioned similar results in his study which showed a significantly low Hb levels in hypertensive disorders of pregnancy as compared to normotensive pregnant.¹⁶ In an Indian study Gajjar *et al* also found association of gestational hypertension with low Hb conc.²²

In previous studies, there is conflicting literature regarding the levels of maternal hemoglobin among hypertensive pregnant women with adverse pregnancy outcomes. It has also been determined that the possibility of low birth weight delivery was increased with the decrease in maternal Hb conc.^{9,23} So, when the anemic pregnancies are associated with hypertensive disorder, these further enhance the threat of maternal, perinatal morbidity and mortality. Endeshaw *et al.* also identified a relationship between anemia and pre-eclampsia.²⁴ A retrospective report from Pakistan in 2019 stated significant influence of anemia on pregnancy-related complications including gestational hypertension.²⁵ Another latest study in 2018 reported that the severity of anemia had a 3.6 times greater risk of pre-eclampsia.¹⁵ Our results findings are also consistent with the above mentioned studies that decrease maternal hemoglobin concentration is significantly related to hypertensive disorders of pregnancy. Interestingly, some earlier studies and meta-analysis by Youngs MF *et al* have demonstrated that a high value of hemoglobin significantly increases the risk for the development of pre-eclampsia.²⁶ This high Hb leads to undesirable pregnancy outcomes.²⁷ Another retrospective cohort study reported that high hemoglobin in pregnant women is related with a high risk of developing PE.²⁸ These results are in contrast to the results of the present study. The variation in the outcome of previous studies can be attributed to different methodology and assorted variables, such as

iron salts supplementation, demographic distinction, low socioeconomic status, poor antenatal care, and hematocrit percentage measured in various trimesters of the pregnancy.⁹

So, the current study has shown a significant relationship between low hemoglobin levels and hypertensive disorders of pregnancy and hence estimates anemia as essential but curable risk factor for hypertensive disorders encountered in gestation. The present study supports the previous studies and shows significant results, but it requires further investigation on large scale because we had small patient population and the data was collected from one center only with no pre and early pregnancy record of Hb values and also no prenatal outcome was documented.

The study limitations were that there was no pre and early pregnancy record of Hb values and also prenatal outcome and the data was collected from one center only. Data from other institutes can further strengthen the results. The results of the present study can be further strengthened if the data is collected from multiple institutes. We only evaluated the third trimester Hb levels. It is, therefore suggested that the Hb levels should be evaluated in all trimesters of pregnancy to further validate the association of Hb levels with the hypertensive disorders of pregnancy.

CONCLUSION

In the present study, the evaluation of Hb shows a statistically significant deterioration in Hb levels among hypertensive pregnant patients as compared to normotensive pregnant women. It can be concluded that timely detection and proper management of anemia in hypertensive disorders of pregnancy can be a key for the prevention and management of hypertensive disorders of pregnancy. Thus, identifying anemic pregnancy which is a curable medical condition will be of great importance in the process of policy making for the early detection and management of hypertensive disorders. For this we must work hard at hospital level as well at community levels to raise awareness regarding controlling and detection of anemia and hypertensive disorder of pregnancy to trim down their associated complications.

ETHICAL APPROVAL: The study protocol was approved by the Institutional Review Board of The University of Lahore. (IRB# IMBB/UOL/18/110).

AUTHORS' CONTRIBUTION: RS: Conception and design, drafting, data collection, Literature search and defining into the vertical content. GM & SQA: Analysis

and intact petition of data, final approval. QA: Revising it for final approval. SJ & NJ: Data entry and collections.

CONFLICT OF INTEREST: The study has no conflict of interest to declare by any author.

FUNDING: None

Received: January 20, 2021

Accepted: March 27, 2021

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