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Original Research Article

A study evaluating third trimester haemoglobin level as a predictor of foeto-maternal outcome in pregnancy induced hypertension cases

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ABSTRACT

Background: The aim of this study is to assess whether third trimester haemoglobin level can be used as a predictor of foeto-maternal adverse outcomes in pregnancies complicated with PIH.

Methods: This is an observational study in the Obstetrics and Gynaecology Department of IMS and SUM hospital, SOA university from July 2015 to December 2017. Institutional ethical committee permission obtained. All singleton pregnancies delivered during this period with PIH were included in the study. PIH and eclampsia was diagnosed as per ISSHP criteria. All chronic hypertension cases excluded. All were evaluated with haemoglobin level. They were divided into 3 groups depending upon haemoglobin level; low (<11gm%), normal (11-13gm%) and high haemoglobin group (> 13gm%) considering the WHO standard. Maternal complications observed were incidence of eclampsia, abruptio placentae, HELLP syndrome, PPH, neurological complications, ICU admissions and death. Fetal outcomes studied were NICU admission, stillbirth, incidence of prematurity and low birth weight. All these parameters were compared among 3 groups. Statistical analysis was done with SPSS 20 software using Yate's corrected chi square test.

Results: Incidence of eclampsia was significantly greater with both high ($p < 0.001$) and low ($p = 0.0085$) haemoglobin level than normal haemoglobin level. Maternal complications and adverse perinatal outcomes (stillbirth, low birth weight, prematurity, NICU admission) are significantly greater with high haemoglobin level than cases with normal haemoglobin level. There is no significant difference in maternal and perinatal complications between low and normal haemoglobin group.

Conclusions: High haemoglobin level >13gm% in third trimester is associated with worst foeto-maternal outcome whereas normal haemoglobin level (11-13gm%) is associated with least foeto-maternal complications.

Keywords: Haemoglobin, HELLP syndrome, NICU admission, Pregnancy induced hypertension, Stillbirth

INTRODUCTION

Plasma volume increases by 40% above pre-pregnancy level in normal pregnancy. Maximum haemodilution is achieved at around 30 weeks, followed by small decrease of haemodilution at term.¹ But, red cell mass increases in a linear fashion with gestation and increase restricted to 25-30% at term.² This physiological hemo-dilution prepares a low viscosity and low resistance intravascular

system which allows an optimal red cell circulation in the low-velocity placental circulation.³ A high haemoglobin concentration during second trimester could be due to ineffective plasma volume expansion or enhanced erythropoiesis as a compensatory mechanism to impaired oxygenation in placenta.^{4,5}

Earlier researches document haemoconcentration with hypovolemia due to ineffective plasma volume expansion

is a feature of pre-eclampsia. A high booking haemoglobin is significantly associated with pre-eclampsia.⁵ Both high haemoglobin (>13.2gm/dl) and low haemoglobin (<10.4gm/dl) are associated with adverse perinatal outcome (preterm delivery, low birth weight, perinatal mortality) in pregnancies not complicated with PIH.⁶

Maternal anaemia is known for adverse maternal and perinatal outcome like postpartum haemorrhage, prematurity, intra uterine growth restriction and low birth weight babies.^{7,8} Not only high haemoglobin, severe anaemia is also associated with a greater risk of preeclampsia.⁹ Risk of adverse outcome in pregnancy is lowest at mid-trimester mean haemoglobin of 11-12gm/dl.¹⁰

Relationship of maternal haemoglobin concentration to maternal and perinatal outcome in a subset of women with PIH has not been observed in many studies. Aim of present study is to find out the relation of haemoglobin level in third trimester with maternal and perinatal outcome in PIH patients. To know, whether third trimester haemoglobin level helps to indicate adverse outcomes in PIH patients.

METHODS

This is an observational study in the Department of Obstetrics and Gynaecology of IMS and SUM hospital, SOA university from July 2015 to December 2017.

Inclusion criteria

311 consecutive patients with singleton pregnancy admitted to in patient department or delivery room with pregnancy induced hypertension were included in the study.

PIH was diagnosed when the systolic blood pressure was ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg measured on 2 occasions 4-6 hours apart beyond 20 weeks of pregnancy. Cases of PIH with convulsion are considered as cases of eclampsia.¹¹

Exclusion criteria

Cases of chronic hypertension like essential hypertension, chronic renal disease, connective tissue disorder were excluded.

Haemoglobin estimation was done for all cases during admission. Haemoglobin estimation in present institute is done by cyanide free Sodium Lauryl Sulphate method, which was uniform in all present cases. All the cases were divided into 3 groups; low haemoglobin group (<11gm%), normal haemoglobin group (11-13gm%) and high haemoglobin group (>13gm%) considering the WHO standard.

Investigations and management were done according to hospital protocol. All cases were evaluated with blood investigations like haemoglobin estimation, platelet count, liver function tests, renal function tests. Coagulation profile (PT, aPTT, INR) was evaluated in clinically suspected cases of abruption, HELLP syndrome, disseminated intravascular coagulation (DIC) patients. Urine protein estimation was done by dipstick method. Obstetric ultrasound with Doppler velocimetry was performed in preterm PIH where decision to continue pregnancy for some period was decided. Admission cardiocography was performed in all cases.

All cases of acute severe hypertension (systolic ≥ 160 mmHg, diastolic ≥ 110 mmHg) were treated with intravenous labetalol preferably or oral labetalol/nifedipine. Any hypertension diastolic ≥ 100 mmHg was treated with oral labetalol/ nifedipine to maintain blood pressure in normal range. All cases of eclampsia, imminent eclampsia (with features like severe headache, visual scotomata, nausea, vomiting, oliguria, epigastric pain) and severe hypertension were treated with magnesium sulphate by Pritchard's regime. Betamethasone 12mg, 24 hours apart administered to all pregnancies less than 37 weeks if imminent delivery is not indicated.

All cases beyond 37 weeks of gestation were planned for delivery. Preterm pregnancies were offered conservative management with the investigations mentioned above twice a week except in cases of eclampsia, imminent eclampsia, uncontrolled maternal hypertension despite antihypertensives, HELLP syndrome, placental abruption, reverse end diastolic flow in Doppler velocimetry, non-reassuring CTG, still birth. Blood pressure monitoring was done 4 hourly for those on conservative management.

All the patients were observed for maternal outcomes like incidence of eclampsia, complications like abruption placentae, HELLP syndrome, postpartum haemorrhage (PPH), neurological complications, intensive care unit (ICU) admission and maternal death. Fetal outcomes studied are described below.

They were described as normal outcome when baby shifted to mother side, neonatal intensive care unit (NICU) admission and stillbirth (delivery of a dead baby after 24 weeks of pregnancy). Incidence of low birth weight (LBW) (<2.5kg), incidence of premature birth (<37 weeks) were observed. All these parameters were compared among 3 groups to see any statistically significant difference exists with different haemoglobin status.

Statistical analysis

Statistical analysis was done with SPSS 20 software using Yate's corrected chi square test.

RESULTS

Total 311 patients of PIH were recruited in the study period. 273 cases out of 311 (87.8%) had pre-eclampsia, 38 (12.2%) cases had eclampsia. Socio-demographic distribution of patients are described below. All PIH patients divided into 3 categories according to the haemoglobin level. 81 candidates in low haemoglobin (<11gm%) group, 181 in normal haemoglobin (11-13gm%) group and 49 in high haemoglobin (>13gm%) group. Table 1 shows age distribution of cases according to haemoglobin level.

Table 1: Age distribution of cases.

Age (years)	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
≤ 20	6 (7.4%)	11 (6.1%)	1 (2%)
21-30	64 (79%)	122 (67.4%)	35 (71.4%)
31-40	10 (12.3%)	48 (26.5%)	13 (26.5%)
>40	1 (1.3%)	0	0

Maximum patients 221/311 (71.1%) are in 21-30 age group. Proportion of patients in this age group is highest in all 3 haemoglobin groups. 64/81 (79%), 122/181 (67.4%) and 35/49 (71.4%) in low normal and high haemoglobin group respectively.

Table 2: Parity distribution of cases.

Study groups	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
Primigravida	58 (71.6%)	113 (62.4%)	33 (67.3%)
Multigravida	23 (28.4%)	68 (37.6%)	16 (32.7%)

Among 311 PIH patients, 204 (65.6%) were primigravidas, 107 (34.4%) were multigravidas. Table 2 compares parity with haemoglobin level. When normal Hb group was compared with high Hb group by chi square test, $p=0.4680$; which is not significant. When normal Hb group was compared with low Hb group, $p=0.1665$; which is not significant. There is no significant difference between the groups, when parity is compared.

Table 3: Distribution of pre-eclampsia and eclampsia.

Study groups	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
Eclampsia	13 (16%)	10 (5.5%)	15 (30.6%)
Preeclampsia	68 (85%)	171 (94.5%)	34 (69.4%)

Table 3 describes distribution of pre-eclampsia and eclampsia among the study groups with different haemoglobin level. According to table 3, proportion of eclampsia, which is the severe form of disease, is highest in high haemoglobin group. It is lowest in normal haemoglobin group. Comparing incidence of

preeclampsia and eclampsia between high and normal haemoglobin group by Fisher's exact test, $p<0.001$; which is extremely statistically significant. Comparing between normal and low haemoglobin group, $p=0.0085$, which is significant.

To present observation, incidence of eclampsia is significantly higher in low and high haemoglobin group compared to normal Hb group.

Table 4: Distribution of maternal complications.

Study groups	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
Normal maternal outcome	75 (92.6%)	176 (97.3%)	39 (79.6%)
Complications	6 (7.4%)	5 (2.7%)	10 (20.4%)

Table 4 illustrates maternal outcome (normal/complications) in 3 study groups. Table 4 depicts maternal complications in different haemoglobin groups. When maternal complications were compared by chi square test between high and normal haemoglobin group, $p=0.0002$, which is highly significant. A higher rate of maternal complications observed in high haemoglobin group than normal haemoglobin group. Contrary, when maternal complications were compared between low haemoglobin and normal haemoglobin group, $p=0.1944$; which is not significant. Present observation suggests maternal complications are highest with haemoglobin level >13gm% and lowest with normal haemoglobin (11-13gm%).

Table 5: Distribution according to gestational age at delivery.

Study group	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
Preterm	22 (27.2%)	46 (25.4%)	23 (46.9%)
Term	59 (72.8%)	135 (74.6%)	26 (53.1%)

Table 5 describes proportion of preterm (<37 weeks) and term (≥ 37 weeks) deliveries among 3 study groups. While comparing high haemoglobin and normal haemoglobin group by chi square test, $p=0.0012$; which is significant. There is no statistical significance between normal and low Hb group ($p=0.7472$). Prematurity is significantly raised with a high haemoglobin level >13gm% than normal haemoglobin (11-13gm%). But, prematurity is not significantly raised in low haemoglobin group, when compared with normal.

Table 6 compares birth weight in different Hb groups. When high and normal Hb group were compared by chi square test, $p=0.0109$; which is significant. LBW neonates between low and normal Hb is not significant ($p=0.774$). LBW neonates are significantly higher with

high Hb concentration than normal. But not with anaemia (low Hb group).

Table 6: Distribution according to birth weight.

Study group	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
Normal birth weight (≥2.5kg)	46 (56.8%)	107 (59.1%)	20 (40.9%)
Low birth weight (<2.5kg)	35 (43.2%)	74 (40.9%)	29 (59.1%)

Table 7 compares perinatal outcome among 3 study groups. Comparing perinatal outcome in high and normal Hb group by chi square test, $p=0.0006$, which is significant. There is no statistically significant difference between low and normal Hb group ($p=0.3312$). Again, worst perinatal outcome in terms of still birth and NICU admission is associated with high haemoglobin level, not with anaemia.

Table 7: Perinatal outcome (normal outcome, stillbirth, NICU admission) among 3 study groups.

Study group	Low Hb (<11gm%) N=81	Normal Hb (11-13gm%) N=181	High Hb (>13gm%) N=49
Normal outcome	57 (70.3%)	142 (78.4%)	26 (53.1%)
NICU admission	18 (22.2%)	26 (14.3%)	14 (28.6%)
Stillbirth	6 (7.4%)	13 (7.1%)	9 (18.3%)

DISCUSSION

Pregnancy induced hypertension is still one of the important causes of maternal and perinatal morbidity and mortality. Hypertensive disorders complicate 5-10% pregnancies globally.¹² Incidence of hypertensive disorders in India is found to be 10.08% as per national eclampsia registry.¹³ Though not preventable completely, identifying cases early and recognising the group prone for serious complications can help reducing maternal and fetal adverse outcomes.

Both high level of maternal haemoglobin and anaemia are associated with PIH.^{6,9} In established preeclampsia, increased capillary permeability and loss of serum protein results in decreased intravascular volume.¹⁴ Decreased plasma volume gives rise to increase in maternal haemoglobin concentration.¹⁵ In pregnancies not complicated with PIH, maternal haemoglobin level correlates with adverse maternal and perinatal outcome.^{6,7,10} In present study, authors are observing any correlation of haemoglobin level in third trimester in PIH patients with maternal and fetal adverse outcomes.

In present observation, incidence of eclampsia, the severe form of disease is significantly greater in high and low haemoglobin group compared to normal Hb group. A stronger association of eclampsia exists with haemoglobin >13gm%. Abnormally high maternal haemoglobin before delivery is associated with placental dysfunction due to high viscosity of blood. Placental ischemia leads to release of placental factors which promotes erythropoiesis. Haemoconcentration initiates peri villous fibrin deposit and placental infarction. A vicious cycle of hypoxia-ischemia- infarction continues which worsens the disease process.¹⁶ Exact reason of raised incidence of eclampsia is not mentioned in studies, probably relates to cerebral hypoxia owing to haemoconcentration, vasoconstriction and cerebral oedema. Significantly higher mean haematocrit value was observed in preeclampsia than normal pregnancy in a cross-sectional study. Statistically significant difference existed between mild and severe PIH as well.¹⁷

Prevalence of preeclampsia and eclampsia is significantly higher in women with severe anemia with Hb concentration <7gm/dl.⁷ The susceptibility of pregnant women with anaemia to PIH may be due to antioxidant and micronutrient deficiency. Reduced serum levels of calcium, magnesium and zinc are possible contributors. In present study, though authors have not categorized anaemic mothers into mild, moderate and severe disease, incidence of eclampsia is significantly higher with low haemoglobin level than normal.

Maternal complications are significantly greater in high haemoglobin group than normal haemoglobin group ($p=0.002$). There is no significant difference between low and normal haemoglobin group. Authors could not find studies correlating Hb level in PIH with maternal outcome. Out of 10 cases of complication in high Hb group, 3 were cases of HELLP syndrome, 3 cases of PPH, 3 cases of neurological complications and one case of maternal death after status eclampticus. 4 cases needed ICU admission among these (2 cases of HELLP syndrome and 2 cases with neurological complication). Low and normal haemoglobin group contain all 6 cases of abruption, 2 cases of HELLP syndrome, 1 case of PPH, 2 cases of neurological complication. Anemia could be the effect of abruptio placentae than the cause. So, it is the high maternal haemoglobin (a state of haemoconcentration and resultant hypoxia) is correlated with most of the complications. Prematurity and low birth weight neonates are significantly higher in high haemoglobin group than normal haemoglobin group. There is no statistical difference between low and normal haemoglobin group. Similar findings observed in other studies where maternal hemoglobin concentration is inversely proportional to birth weight percentile in PIH.^{18,19} In a study by Sagen N et al, the last maternal haemoglobin concentration before delivery was correlated with perinatal outcome. Abnormally high Hb was associated with placental dysfunction, intrauterine

fetal growth restriction, perinatal distress and higher rate of perinatal death.¹⁹

Mean maternal haemoglobin concentration between 11.0 and 12gm/dl in 2nd trimester had lowest risk of any adverse perinatal outcome. A possibility of adverse event was highest between haemoglobin 13.0-15gm/dl.¹⁰ Low birth weight, perinatal mortality, and prematurity were significantly higher in cases where mid trimester Hb was more than 13.2gm/dl.⁶ Authors could not find any statistical significance between low and normal Hb group when considered for perinatal outcomes. Lowest incidence of low birth weight and preterm labour was associated with haemoglobin concentration 95-105gm/L which can be considered as low Hb according to WHO standard.³ In a large prospective European study, perinatal mortality was lowest with a haemoglobin range of 9-11gm/dl in first antenatal checkup.²⁰ U-shaped curve of increased risk by haemoglobin level for adverse birth outcomes (stillbirths, preterm deliveries, SGA) was observed in another study. The optimal haemoglobin level, with the lowest perinatal risk, was between 11 and 13 g/dl.²¹ High haemoglobin at first antenatal visit (>14.6gm%) is associated with increased risk of still birth according to a population based Swedish study.²²

CONCLUSION

Pregnancy induced hypertension is associated with adverse maternal and perinatal outcomes. Early detection, segregation of cases prone for worst outcome and timely proper intervention can improve the outcomes.

From present study, it is clear that haemoglobin measurement in third trimester in PIH patients can be used as an indicator of maternal and fetal adverse outcomes.

Normal haemoglobin level between 11 and 13 gm% is associated with least maternal complications like eclampsia, maternal morbidity and mortality. Fetal complications like prematurity, low birth weight, NICU admission, stillbirth rate were lowest with this haemoglobin level.

Worst maternal and fetal outcomes are associated with haemoglobin level more than 13gm%. Anaemic mothers (Hb<11gm%) are prone to moderate level of maternal and fetal complications between high and normal haemoglobin.

Haemoglobin level is performed in all present obstetric cases as part of routine investigation. Without increasing the cost or burden on health care, it can be used as an indicator of adverse fetomaternal outcome.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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