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A Comparative Study of Cord Blood Hematological Profile of Neonates Born to Mothers with and without Pregnancy - Induced Hypertension

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Abstract: ***Aim**: The purpose of this study was to compare the haematological profile of cord of neonates born to mothers with and without PIH, and to evaluate short term clinical outcomes in the two groups. **Methods**: A prospective case control study was done on cord blood of 50 neonates born to mother with PIH (cases) and compared with 50 neonates born to normotensive mothers (controls) attending OPD/Labour room/Ward of Department of Obstetrics &Gynaecology SRMSIMS, Bareilly. 2 ml cord blood was collected from the placental end at the time of delivery and was analysed for haemoglobin, PCV, various red cell indices, nucleated RBC, reticulocyte count, total leucocyte count, differential leucocyte count and platelet count. The cases and controls were followed up during their hospital stay for clinical outcome. Data was analysed using software IBM SPSS statistics version 20.0 and was compared using Chi-square test. **Results**: Platelet count was found to be significantly lower whereas mean corpuscular volume, reticulocyte count, nucleated RBC, lymphocytes and monocytes were significantly increased in neonates born to mothers with PIH. There was significantly higher incidence of respiratory distress and NICU admission in neonates of mothers with PIH. **Conclusion**: It was concluded that there are significant differences in haematological profile of neonates born to mothers with and without PIH. A positive association was seen between PIH and neonatal thrombocytopenia which was in accordance with results of most studies. The relationship of mean corpuscular volume, reticulocyte count and nucleated RBC in neonates of PIH mother ties well with most studies whereas in case of lymphocytes it was non-comparable with other studies. **Clinical significance**: Neonates of hypertensive mothers should be carefully evaluated and monitored in terms of haematological abnormalities. Following up these neonates may give us more insight in the progression of hematological derangements that can further guide management and establish whether there is a need to institute screening all neonates born to hypertensive mothers. We believe that a multidisciplinary, collaborative approach between the fields of maternal-fetal medicine and neonatology is necessary to weigh the maternal and fetal risks of prolonging the pregnancy versus the potential benefits of further fetal maturation across most gestational ages.*

Keywords: pregnancy induced hypertension, thrombocytopenia, haematological profile, Apgar score, fever, respiratory distress, NICU admission

1. Introduction

Hypertensive disorders are the commonest medical problem during pregnancy. Gestational hypertension, is a condition characterized by high blood pressure during pregnancy {systolic blood pressure (SBP) >140 mm Hg and diastolic blood pressure (DBP) >90 mmHg}.[(1,2)] PIH is produced by maternal and placental vascular dysfunction and mostly disappears after delivery. However, more than 80% cases grow at term with good maternal and fetal consequences; these pregnancies are still at higher risk for maternal and/ or fetal mortality or serious morbidity. Moreover, women with preeclampsia are also at higher risk for future cardiovascular, renal and chronic hypertensive disease.[(3)]PIH occurs because of any of the four conditions[(2)]:

Classification of hypertension in pregnancy[(4)]

- Preeclampsia and Eclampsia syndrome
- Chronic hypertension of any etiology
- Preeclampsia superimposed on chronic hypertension
- Gestational hypertension

Maternal hypertension changes the intrauterine atmosphere of the fetus and the fetus has to acclimatize to living in the unfavorable environment. These effects comprise higher neonatal mortality and morbidity, intrauterine growth restriction (IUGR), premature birth, necrotizing enterocolitis, and hematological abnormalities (such as thrombocytopenia, polycythemia, and neutropenia). Neonates of hypertensive mothers were more liable to have lower WBC and thrombocytopenia and this danger increase when the mothers develop preeclampsia.[(5)]

Derangement of hematological parameters was one of the complications suffered by neonates of hypertensive disorders of pregnancy with neutropenia and thrombocytopenia being the most commonly found hematological imbalances in newborns. Changes had been found in the hematological parameters of newborns of hypertensive and normotensive mothers. These differences were mainly seen in Hemoglobin, red cell distribution width

(RDW), packed cell volume (PCV) mean cell volume (MCV), red cell count, neutrophil counts and platelet counts.

Aim
To compare the hematological profile of cord blood of neonates born to mothers with and without Pregnancy induced hypertension (PIH).

2. Material and Methods

Place of Study: Department of Obstetrics and Gynecology, Shri Ram Murti Smarak Hospital, Bareilly.

Population of Study: All patients fitting the inclusion criteria consenting for the study attending the in-patient department at SRMS IMS Hospital in the Department of Obstetrics and Gynecology.

Study Design: Prospective case study

Sample Size: Total 100 patients included in study, where 50 patients of Pregnancy induced hypertension and 50 patients with Normotension.

Study Period: November 2018 – May 2020.

Inclusion Criteria:
- Neonate born to pregnant women with pre-eclampsia or eclampsia, Gestational Hypertension were included as study case.
- Neonate born to normotensive mother without any complication were included as control.

Exclusion Criteria:
- Maternal and fetal morbidity and mortality which ones Rh- incompatibility, Diabetes mellitus, twin-pregnancies.
- Medical illness: Renal disease, Heart disease, connective tissue disease.
- Those who received drugs such as aspirin which are likely to cause changes in hematological profile
- Chronic hypertension
- Neonates with significant congenital malformations
- Severe perinatal asphyxia in the neonate

Study Technique
After selecting the cases from IPD and wards, detailed history of the woman was documented in the pre-designed case proforma. Neonates born to mothers with gestational hypertension, pre-eclampsia or eclampsia was included as study group and neonates born to normotensive mothers without any complications was taken as controls.

The pregnant females was diagnosed as having PIH, based on the working group (National High Blood Pressure Education Program) definition and American College of Obstetricians and Gynecologists criteria:
1) BP ≥ 140/90 mmHg.
2) Proteinuria > 1+ on dipstick urine protein testing.
3) Edema (Present/Absent)
4) Seizures. (Present/Absent)
5) In the absence of proteinuria, thrombocytopenia (<100000 platelets/cu mm), oliguria (<400 ml urine in 24 h) and/or impaired renal functions, persistent headache and visual symptoms, epigastric pain and/or impaired liver functions, respiratory distress, and cyanosis (pulmonary edema) were looked for, to establish the diagnosis of pre-eclampsia.

Maternal data such as age, parity, antenatal visits, gestational age, onset of symptoms, BP recording and presence of seizures and proteinuria was noted. Details of labor including mode of delivery, duration of labor, rupture of membranes, and presence of any complications during labor was recorded.

Neonatal data such as sex, date of birth, time of birth, weight, Apgar scores at 1 and 5 min, NICU admission were noted. Any complications following short hospital stay were noted.

Specimen to be collected: At birth, 2 ml cord blood was collected in the ethylene diamine tetra acetic acid (EDTA) vial and analyzed (within an hour) for hemoglobin (Hb), red cell indices such as Packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), MCH concentration (MCHC), red cell distribution width (RDW), nucleated red blood cell (NRBC) count, reticulocyte count, total leukocyte count (TLC), differential leukocyte count (DLC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count, and cord blood smear examination. Hb, PCV, MCV, MCH, MCHC, RDW, TLC, DLC, and platelet count was estimated using automated cell counter method. General blood picture and nucleated RBCs (per 100 white blood cells) was examined using the smear stained with Fleishman's stain, under Nikon E 100 microscope. For reticulocyte count, the smear was stained with methylene blue (supravital stain) and examined under oil immersion (×100).

After completion of data collection, all the data were entered in MS Excel spreadsheet and analyzes with the help of software IBM SPSS version 20.

3. Observations

1) Age wise distribution of pregnant women in both groups

Age (Years)	Group A n=50 (%)	Group B n=50 (%)	Total n = 100 (%)
≤ 20	5 (10.0)	4 (8.0)	9 (9.0)
21 – 25	30 (60.0)	28 (56.0)	58 (58.0)
26 – 30	10 (20.0)	14 (28.0)	24 (24.0)
> 30	5 (10.0)	4 (8.0)	9 (9.0)
Mean ± SD	24.6 ±3.8	25.0 ± 3.8	
Minimum	19	20	
Maximum	33	36	

In present study, mean age of the patients in group A was 24.6 ± 3.8 years with minimum age 19 years and maximum age of 33 years, while among Group B is mean age was 25 ± 3.8 years with minimum age 20 years and maximum age 36 years .

2) Distribution of Pregnant women based on Gravida status

Gravida status	Group A(%)	Group B (%)	Total (%)
Primigravida	30 (60.0)	16 (32.0)	46 (46.0)
Second gravida	11 (22.0)	18 (36.0)	29 (29.0)
Third gravida	6 (12.0)	9 (18.0)	15 (15.0)
Fourth or more gravida	3 (6.0)	7 (14.0)	10 (10.0)
Total	50 (100.0)	50 (100.0)	100 (00.0)

Regarding obstetric history, in Group A (n=50), majority of the patients (60%) were primigravida. While in Group B (n=50), more than one-third of the patients (36%) were second gravida pregnancy, followed by primigravida (32%).

3) Distribution of pregnant women based on Type of PIH

Type of PIH	No of patients	Percent
Gestational hypertension	27	54.0
Preeclampsia	21	42.0
Eclampsia	2	4.0
Total	50	100.0

Among Group A (n=50), 54% of women were suffering from gestational hypertension, while 42% from preeclampsia and 4% suffering from eclampsia.Also in Group A (n=50), 84% patients had no postpartum complication, while 16% patients had PPH. However, in Group B (n=50), 94% patients had no postpartum complication, while 6% patients had PPH.

In Group A (n=50), 24% pregnant women delivered LBW babies (<2.5 kg) and 76% delivered normal birth weight babies (2.5-4.0 kg). In Group B (n=50), 22% women delivered LBW babies and 78% delivered normal weight babies .In Group A (n=50), 78% newborn babies had APGAR score of ≥7 at 1 minute and 22% had <7 APGAR score at 1 minute. While in Group B (n=50), 96% babies had ≥7 APGAR score at 1 minute and 4% had <7 APGAR score at 1 minute.

4) Distribution based on NICU admission of newborn

Table 4: Distribution of both groups based on NICU admission of newborn

NICU admission of newborn	Group A (%)	Group B (%)	Total (%)
Present	9 (18.0)	1 (2.0)	10 (10.0)
Absent	41 (82.0)	49 (98.0)	90 (90.0)
Total	50 (100.0)	50 (100.0)	100 (100.0)

Among Group A (n=50), 18% newborn required NICU admission, though among Group B (n=50), 2% newborn required NICU admission.

5) Distribution based on Complete blood count of newborn

Complete blood count	Group A (Mean ± SD)	Group B (Mean ± SD)	P value
Hematocrit (%)	48.68 ± 6.98	48.63 ± 15.17	0.983
Hemoglobin (gm/dl)	15.88 ± 2.68	15.65 ± 5.04	0.776
White blood cells (per µL)	10024 ± 17772	11757 ± 6141	0.516
Platelet count (lakhs/µL)	1.01 ± 0.80	2.28 ± 1.03	*<0.001*
Reticulocyte count (%)	7.34 ± 2.50	3.50 ± 1.44	*<0.001*
Nucleated RBC (million/mm^3)	12.36 ± 2.98	4.64 ± 2.81	*<0.001*
MCH (picogram/cell)	32.73 ± 3.70	32.54 ± 4.95	0.823
MCV (femtoliters/cell)	107.3 ± 8.6	101.8 ± 8.5	*0.002*
MCHC (gm/dL)	33.05 ± 1.41	33.39 ± 1.42	0.232

Mean values of **Hematocrit** was non-significantly higher among newborns of Group A (48.68±6.98 %) comparing to newborns of Group B (48.63±15.17 %) {p>0.05}. Mean values of **Hemoglobin**was non-significantly higher among newborns of Group A (15.88±2.68 gm/dl) comparing to newborns of Group B (15.65±5.04 gm/dl) {p>0.05}. Mean values of **White blood cells (WBC) count** was non-significantly lower among newborns of Group A (10024±17772 per µL) comparing to newborns of Group B (11757±6141 per µL) {p>0.05}. Mean values of **Platelet count**was significantly lower among newborns of Group A (1.01±0.8 Lakhs/µL) comparing to newborns of Group B (2.28±1.03Lakhs/µL) {p<0.05}. Mean values of **Reticulocyte count** was significantly higher among newborns of Group A (7.34±2.5 %) comparing to newborns of Group B (3.5±1.44 %) {p<0.05}. Mean values of **Nucleated RBC (Red blood cell) count** was significantly higher among newborns of Group A (12.36 ± 2.98 million/mm^3) comparing to newborns of Group B (4.64 ± 2.81 million/mm^3) {p<0.05}. Mean values of **Mean corpuscular hemoglobin (MCH)** was non-significantly higher among newborns of Group A (32.73±3.7 picogram/cell) comparing to newborns of Group B (32.54±4.95 picogram/cell) {p>0.05}. Mean values of **Mean corpuscular volume (MCV)** was significantly higher among newborns of Group A (107.3±8.6 femtoliters/cell) comparing to newborns of Group B (101.8±8.5 femtoliters/cell) {p<0.05}.Mean values of **Mean corpuscular hemoglobin concentration (MCHC)** was non-significantly higher among newborns of Group A (33.05±1.41 gm/dL) comparing to newborns of Group B (33.39±1.42 gm/dL) {p>0.05}.

6) Distribution based on Differential counts of WBC of newborn

Differential counts of WBC	Group A (Mean ± SD)	Group B (Mean ± SD)	P value
Neutrophils	60.95 ± 18.50	67.02 ± 12.29	0.056
Lymphocytes	34.19 ± 16.98	26.24 ± 5.04	*0.009*
Eosinophils	2.70 ±2.09	3.19 ±2.03	0.241
Monocytes	2.09 ±1.41	1.48 ± 1.66	*0.049*
Basophils	0.02 ±0.14	0.18 ±0.87	0.204

Mean percent of **Neutrophils** was non-significantly lower among newborns of Group A (60.95±18.5 %) comparing to newborns of Group B (67.02±12.29 %) {p>0.05}. Mean percent of **Lymphocytes** was significantly higher among newborns of Group A(34.19±16.98 %) comparing to newborns of Group B (26.24±5.04 %) {p<0.05}. Mean percent of **Eosinophils** was non-significantly lower among newborns of Group A (2.7±2.09 %) comparing to newborns of Group B (3.19±2.03 %) {p>0.05}. Mean percentof **Monocytes** was significantly higher among newborns of Group A(2.09±1.41 %) comparing to newborns of Group B (1.48±1.66 %) {p<0.05}. Mean percent of **Basophils** was

non-significantly lower among newborns of Group A (0.02±0.14 %) comparing to newborns of Group B (0.18±0.87 %) {p>0.05}.

4. Discussion

In present study, majority of the patients belonged to low socio-economic class in group A (66%) and group B (72%). As many factors are accounting for socioeconomic status so we can say socioeconomic status may affect the study outcome. Both groups are comparable in reference to socio-economic status. A similar conclusion was reached by **Meher et al**(2017) in which higher number of cases (60%) belonged to low socio-economic status as compared to controls (50%).[6]

Among study population group A, 54% patients had gestational hypertension, 42% preeclampsia and 4% eclampsia. This observation is comparable to that of **Kheir et al** (2014) who noted that among 69 patients, 42% had gestational hypertension, 21.7% had preeclampsia, 4.3% had eclampsia and 20.2% had chronic hypertension.[7] In group A, 22% newborns had <7 APGAR score at 1 minute, while 4% had <7 APGAR score at 5 minutes. Conversely in group B, 4% newborns had <7 APGAR score at 1 minute, while none had <7 APGAR score at 5 minutes. The relationship of APGAR score between group A and group B was statistically significant at 1 minute (p<0.05), but statistically not-significant at 5 minutes (p>0.05), i.e. it was comparatively less in group A than group B at 1 minute of life and later on improved with resuscitation. This result is partly comparable with a study by **Darkhaneh et al** (2013) who found that average 1st and 5th minutes Apgar scores was significantly higher in normal mothers as compared to preeclamptic mothers (p<0.001).[8]

In our study, among newborns of group A, mean values of Hematocrit, Hemoglobin were non-significantly higher, while WBC count was non-significantly lower than those of control. In differential count of WBC the mean percentage of Lymphocytes (p=.009) and Monocytes (p=.049) were significantly higher whereas those of Neutrophils, Eosinophils and Basophils were non-significantly lower as compared to newborns of group B (p>0.05). Further in newborns of group A, mean values of Reticulocyte count, Nucleated RBC count were significantly higher (p<.001) than control, while Platelet count was significantly lower as compared to newborns of group B (p<0.001). On the basis of above observations we can infer that the hemoglobin, hematocrit and WBC count were comparable between neonates of both group. But there was significant thrombocytopenia in newborn of patients with PIH. Besides, the reticulocyte count and the nucleated RBC were significantly higher in the neonates of PIH patients. When RBC indices were compared, only MCV was significantly higher (p=.002) in the neonates of group A whereas MCH and MCHC were comparable between the two groups. This may be due to inability of cytotrophoblasts to differentiate correctly, leading to failure of its invasion of spiral arterioles into the uterus. This relatively leads to hypoxic environment in the placenta resulting in increased production of erythropoietin which in turn leads to stimulation of erythropoiesis and thereby increased number of nucleated RBC. Therefore, increased count of nRBC is considered as a marker of hypoxia. Increase in reticulocyte is mainly due to high erythropoietic stimulus to face a higher RBC destruction and removal.

A similar pattern of results was obtained by **Eman et al** (2017) who found that difference in mean values of Hemoglobin, PCV, MCV, MCH, and MCHC of neonates born to PIH cases and controls were not statistically significant (p>0.05).However, the difference in mean values of nucleated RBCs, RDW, reticulocyte count and leukocyte indices (TLC, ANC and ALC) and incidence of leukopenia and absolute neutropenia between cases and controls was statistically significant (p<0.05). The platelet counts and incidence of thrombocytopenia between cases and controls were also significantly different (p<0.05). There was significant correlation between severity of maternal hypertension and neonatal platelet count in the cases (p<0.05).[9] **Prakash et al** (2013) noted that number of nucleated RBCs seen in the peripheral smear was significantly higher in babies born to mother with hypertensive disorders. While total WBC count, neutrophil count, absolute neutrophil count and platelet count were significantly decreased in babies of PIH pregnancy. There was a significantly higher MCV, while the RBC and the MCH were only suggestive of statistical significance between the cases and the controls.[10]

5. Conclusion

It can be observed from our study that there are significant differences in hematological profile of neonates born to mothers with and without PIH. There was a positive association between PIH and thrombocytopenia, which may be related to intrauterine hypoxia with subsequent suppression of megakaryocyte proliferation.

The results show increase lymphocytes in cord blood of women with PIH which suggests an imbalance in immune cells of PIH mothers. Further, it was found that there is increased MCV, reticulocyte count and the nucleated RBC in newborn of PIH patients as compared to normotensive mothers. Thus, newborns of hypertensive mothers carry a risk for both infection and bleeding in early neonatal life.

Hence, it is recommended that regular antenatal care should be encouraged more preventive and therapeutic measures for pregnancy induced hypertension. Complete blood counts are significant widely available, low cost laboratory tests, which can be used for early diagnosis of hematological complications in newborns of PIH mothers. Following up these neonates may give us more insight in the progression of these derangements that can further guide to manage and establish whether there is a need for screening all neonates born to hypertensive mothers.

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