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"COMPARISON OF COAGULATION PROFILE IN THE NEWBORNS OF PREGNANCY INDUCED HYPERTENSIVE MOTHERS WITH COAGULATION PROFILE IN THE NEWBORNS OF NORMOTENSIVE MOTHERS"

Hematology

Dr. Rabia Parveen Siddiqui Professor, Department Of Pathology, Pt. Jawaharlal Nehru Memorial Medical College (Pt. JNMMC), Raipur, Chhattisgarh, India

Dr. Shashikala Kosam Associate Professor, Department Of Pathology, Government Medical College, Mahasamund, Chhattisgarh, India

Dr. Deepa Janghel Demonstrator, Department Of Pathology, Lt. Bisahu Das Mahant Memorial Medical College (GMC), Korba, Chhattisgarh, India

Dr. Shende Pranali Kisandas* Senior Resident, Department Of Pathology, GMC, Chandrapur, Maharashtra. *Corresponding Author

ABSTRACT

Background & Objectives: Hypertensive disorders of pregnancy, includes pre-existing and gestational hypertension, preeclampsia and eclampsia; complicating upto 10% of pregnancies. In Pregnancy induced hypertension (PIH), localized coagulation fibrinolytic imbalance has been reported; which increases the risk of preterm deliveries and low birth weight babies & rendering the babies at risk of bleeding and increased susceptibility to infection due to reduction of platelets number and impaired coagulation profile. The Objective of this study was to compare the nature and extent of variations in coagulation profile in newborns of PIH mothers with that of coagulation profile of newborns of normotensive mothers. **Methods:** Observational Analytical study was carried out for one year at Pathology Department, Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh (CG) under **Control group-** newborns delivered to Normotensive mothers & Study group- newborns delivered to Gestational Hypertensive, Preeclamptic & Eclamptic mothers. **Results:** Compared to newborns of normotensive mothers, newborns of PIH mothers showed increasing severity of thrombocytopenia; prolongation of PT, APTT, TT & detectable FDP in the serum with increasing severity of PIH. **Interpretation & Conclusions:** Thrombocytopenia with deranged coagulation profile in newborns of PIH Mothers could be explained by DIC & require close follow-up for management of these newborns. We conclude that estimation of coagulation parameters can be considered as an early & rapid procedure in the assessment of effect of severity of PIH on the newborns & hence their management for preventing morbidity and mortality.

KEYWORDS

APTT, Coagulation, FDP, Newborns, PIH Mothers, PT, Thrombocytopenia, TT

INTRODUCTION:

Pregnancy induces complex changes which are concerned with hemostasis. Normal pregnancy is associated with hypercoagulable state which becomes more pronounced at term while in pre-eclampsia or Pregnancy induced hypertension (PIH) localized coagulation fibrinolytic imbalance has been reported. Hypertensive disorders of pregnancy complicate up to 10% of pregnancies and represents a significant cause of maternal and perinatal morbidity and mortality.[1,2,3] PIH in antenatal women increases the rate of Cesarean sections, increased risk of preterm deliveries and low birth weight babies.[4,9,10,11,12,13,15] There were significant changes in the hematological profile & coagulation profile rendering the babies at risk of bleeding and increased susceptibility to infection due to reduction of platelets number and impaired coagulation profile.[8,9,11,14] Preterm baby has proven to be more affected than full term. [5,6,7,8] All these findings suggest a need of good antenatal care and resuscitation facilities and careful follow up of hematological and coagulation status for this group of babies. This study is undertaken in a view to compare the Coagulation Profile in Newborns of PIH mothers as early detection of these abnormalities can help in prevention of significant mortality in the newborns of PIH mothers. Aim of the study was to compare the nature and extent of variations in coagulation profile in newborns of PIH mothers with that of coagulation profile of newborns of normotensive mothers.

MATERIAL & METHODS:

It was an Observational Analytical - Case control study. It was conducted in the Department of Pathology, Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh (CG), India over period of One year {January, 2019 to December, 2019}. A total of 228 subjects were studied as Sample size = 76, Study being case control (1:2). The materials for the study consisted of samples from Total number of 228 newborns of pregnant women admitted & delivered in Obstetrics & Gynecology labor room & Operation Theater of this hospital. The study was carried out in the two groups. Group I: Control group included 152 newborns delivered to Normotensive mothers. Group II: Study group included 76 newborns delivered to Gestational Hypertensive, Preeclamptic & Eclamptic mothers. Ethical clearance was obtained from the Institutional Ethical Committee for conducting the study. The details of the study were explained to the subject's caregivers and written informed consent were taken from mothers / Caregivers of subjects under study. We included cases as per selection of cases done with the help of Obstetricians, after taking detailed history & going through clinical examination i.e newborns of PIH & Normotensive mothers & excluded Pregnant women with Previous history of Haemorrhagic Disorders, Drug intake affecting platelet & fibrinogen, Epilepsy, Diabetes Mellitus, Renal Disease. With above mentioned criteria, study group was further divided in Group 2- Newborns of Gestational Hypertensive Mothers Group 3- Newborns of Preeclamptic Mothers Group 4- Newborns of Eclamptic Mothers.

Collection of Materials:

From newborns (study subjects) with all aseptic precautions 5ml Cord Blood sample was drawn from the umbilical vein before placental separation after the cord was clamped and cut. A single puncture was made and care was taken to obtain the samples within seconds in 10ml sterile plastic syringe with 19 or 20 S.W.G needle and collected in a vacutainers containing: a) 3.2% buffered sodium citrate to measure coagulation profile:- Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT), and serum Fibrin / Fibrinogen Degradation Products (FDP) assay. b) 5.4mg K2 Ethylenediaminetetraacetic Acid (K2 EDTA) for platelet count. Mixed gently. Centrifuged immediately for 15 min at 3000 rpm to get platelet poor plasma. Transferred supernatant plasma in plastic tube immediately; not disturbing the buffy coat while collecting supernatant plasma. The tests were done within 2 h of blood collection. All pipetting were performed by using automatic pipette & disposable tips. The investigations were performed as follows: a) Platelet count [based on principle of Impedance resistance]- By Automated Haematology Analyser Beckman Coulter using samples collected in a K2 EDTA vacutainer whereas based on opto-mechanical measuring principle b) Prothrombin time (PT), c) Activated Partial Thromboplastin Time (APTT) & d) Thrombin Time (TT) by automated blood coagulation analyser MISPACLOG using samples collected in a 3.2% buffered sodium citrate vacutainer from which platelet poor plasma was obtained & lastly Fibrinogen degradation products (FDP) assay [Latex Agglutination] also from obtained platelet poor plasma.

Results: The results were analysed by various statistical techniques like percentage, mean, standard deviations, t-test and test of significance ($\chi 2$) whichever were found necessary.

Table-I: Distribution of Subjects into Study Subgroups and Control group

Distribution of Subjects	Number	%
Newborns of Normotensive / Control Mothers (N)	152	67
Newborns of Gestational Hypertensive Mothers (GHD)	32	14
Newborns of Preeclamptic Mothers (PE)	25	11
Newborns of Eclamptic Mothers (E)	19	08
Total	228	100

Table-II: Variations in Coagulation profile of Total number of Newborns of Study subgroups and Control group

Assay	Control (Mean ± SD)	Cases (Mean ± SD)	P-value
Platelet Count	256.29 ± 77.49	189.78 ± 79.94	0.001
PT	16.51 ± 4.51	19.53 ± 5.68	0.001
APTT	52.29 ± 8.15	72.48 ± 12.38	0.001
TT	20.70 ± 2.78	25 ± 3.5	0.001

DISCUSSION:

Hypertensive disorders of pregnancy have been associated with increased perinatal morbidity & mortality as it predispose women to acute or chronic uteroplacental insufficiency, there by having an effect on perinatal & neonatal outcome that may result in ante 0r intra partum anoxia that may lead to foetal death, intrauterine growth retardation &/or preterm delivery. Some studies have shown that there is an increased incidence of birth asphyxia, transient tachypnoea of newborn (TTNB), hyaline membrane disease (HMD) & neonatal sepsis with significant changes in hematological profile & coagulation profile in newborns of these mothers. El Sayed MA, Ahmed A et al (2018), mean age of study group was 27.9 ± 4.03 years and that of control group was 27.6 ± 3.9 years which is slightly higher than our study.[7] Sivakumar S, et al (2015), mean age of study group was 24.3 years and that of control group was 23.38 years which is comparable with our study.[5] Younger age has been described as risk factor for PIH in many studies. Extreme age ranges have also been associated with increased incidence of PIH. In our study also maximum newborns were of mothers of younger age group 21–25years. Sivakumar S, et al (2015), mean gestational age of mothers in study group was 37.4 weeks and that of control group of mothers was 38.6 weeks which was comparable with our study.[5] It was apparent that as the severity of PIH increased, the gestational age decreased. El Sayed MA, Ahmed A, et al (2018), Sivakumar S, et al (2015), Meher P, et al & Bhat YR, et al (2008) also have maximum subjects born to as Primigravidae which was same as our present study.[7,5,18] Primigravida has been described as a major risk factor for PIH. Probably the young age group being the commonest age of presentation in PIH may be responsible for preponderance of primigravida cases. Although the exact pathophysiologic mechanism is not known; it was reported that utero-

Table-III: Variations in Coagulation profile of Normotenive and PIH mothers Newborns

Assay	Study Subgroups Newborns of PIH Mothers			Control / Newborns of Normotensive	F-value	P-value
	GHD	PE	E			
PC	202.47 ± 77.73	161.4 ± 63.29	205.7± 95.96	256.29 ± 77.49	13.99	0.001
PT	17.79 ± 3.95	21.66 ± 4.17	19.63± 8.54	16.51 ± 4.51	9.48	0.001
APTT	65.57 ± 8.9	75.12 ± 9.06	80.65± 15.01	52.29 ± 8.15	94.94	0.001
TT	23.84 ± 3.2	25.72 ± 3.15	26 ± 4.26	20.70 ± 2.78	36.58	0.001

Table- IV: FDP assay in Study subgroups and Control group

Subjects	<200ng/ml / Nil	>200ng/ml	Total
Newborns of Normotensive /Control group	121	31	152
Newborns of Gestational Hypertensive Mothers	19	13	32
Newborns of Preeclamptic Mothers	12	13	25
Newborns of Eclamptic Mothers	04	15	19
Total	156	72	228

placental insufficiency secondary to pregnancy induced hypertension is responsible for the development of thrombocytopenia in newborns. Combined effect of impaired megakaryocyte formation and increased platelet activation mediated through cytokines, thrombopoietin and IL-6 were said to be the most likely causative mechanisms. Thrombocytopenia could occur as a result of thrombocyte adherence to the damaged endothelial region caused by segmental vasospasm and vasodilatation in the placenta of hypertensive mothers.[7,8] The rate and severity of thrombocytopenia in neonates of PIH mothers varies. Purnima Meher et al., proved higher incidence of thrombocytopenia in newborns of preeclamptic mothers compared to the newborns of normotensive mothers.[9] Kleckner et al. reported that abnormal placental endothelial surface caused thrombocytes destruction and the resulting thrombocytopenia.[19] Thrombocytopenia is the result of placental insufficiency and decreased production; however Samuels et al. have demonstrated abnormal platelet antibodies in the infants of preeclamptic mothers and considered an immune theory. There are studies that support the role of mediators in developing thrombocytopenia. Normally, vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) are responsible for maturation of megakaryocyte and participate in the regulation of megakaryocyte development. Low levels of PIGF and VEGF are shown in the cord blood of preeclamptic mothers' babies. Thrombocytopenia is a transitory alteration, more commonly found in the first 72 hours after birth, with resolution within 10 days and was not severe in most cases.[14] Developmental hepatic immaturity and impairment of balance between coagulating and fibrinolysis at uteroplacental circulation, the maturity status of preterm babies to preeclamptic mothers were found to have more compromise in their coagulation panel. Thus, immaturity of the liver and haemostatic system could be the major cause. Narayan et al, had reported similar results and they attribute their results to sever vitamin k deficiency in preterm ones.[7,17] Severe hypertension may result in a marked imbalance in the hemostatic system both in the mother and infants. Prolongation of PT, PTT and TT was demonstrated by Narayan et al. & one reason for this derangement may be the lack of balance between coagulation and fibrinolysis in localized area of vascular compartment especially uteroplacental circulation.[14] To address the hypothesis that infants with extreme APTT prolongation might exhibit reduced thrombin generation. The fetal coagulation system matures with GA. Coagulation factor synthesis begins in utero at approximately 10 gestational weeks, increasing with advancing gestation into the postnatal period, and reaching adult levels by 6 months of age. Moderately premature infants have reduced plasma concentrations of both procoagulant and anticoagulant vitamin K-dependent clotting factors compared with term infants. However, plasma levels of other proteins, including FXII and contact pathway factors, are also reduced.[7,8] Neonates have lower levels of vitamin K- dependent clotting factors compared with term infants & APTT assay is sensitive to reduced plasma activity of these factors. Moreover, the APTT was also prolonged by reductions in FXII and contact pathway factors, neither of which were associated with a bleeding tendency or reduced thrombin generation. Reduction in these contact pathway factors had been well characterized in older preterm infants.[16] Narayan S, et al (1994) found serum FDP levels were raised in 60% cases in study group. Derangements were more pronounced in neonates born to severe PIH mothers than in mild PIH especially in preterm babies.[17]

CONCLUSION:

The low platelet count with prolongation of PT, APTT, TT and raised serum FDP levels in newborns could be explained by DIC. Hence, neonates of PIH mothers who may be at an increased risk for bleeding disorder & may require close follow-up and further studies are suggested to see the modalities of management of these newborns. We found that among all the coagulation parameters in the newborns, APTT & TT were prolonged significantly with severity of PIH in the mothers & should be assessed as marker for predicting the effect of severity of PIH on the coagulation parameters of newborns & hence their management. Further studies are needed to explore the usefulness of these parameters. We conclude that estimation of all coagulation parameters can be considered as an early & rapid procedure in the assessment of effect of severity of PIH on the newborns & hence their management for preventing morbidity and mortality.

Conflicts of Interest: Nil.

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