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Research Article

Maternal and Cord Blood Nucleated Red Blood Cell Count in Pre-Eclampsia and Normal Pregnancy - A Comparative Study

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Abstract: Pre-eclampsia is considered to be a state of deterioration of utero–placental perfusion and is associated with inadequate blood supply to the fetus, which can result in chronic hypoxia; as a result it enhances the production of NRBC in the fetus. The aim of this study was to evaluate the influence of pre-eclampsia on the cord and maternal nucleated red blood cell (NRBC) count. The method was immediately after delivery, 1 mL of maternal venous blood and 1 mL of cord blood from 120 pre-eclamptic and 120 healthy pregnant women were collected and the number of NRBC per 100 leukocytes in maternal and cord blood was counted and compared between the two groups. Any correlation of the NRBC count in maternal and umbilical cord blood with severity of pre-eclampsia was also evaluated. In results the mean Maternal NRBCs/100 WBCs was 5.85 ± 4.022 in Group-A as compared to 2.33 ± 2.571 in Group- which was statistically significant. The mean cord blood NRBCs in Group-A was 16.19 ± 7.052 and mean cord blood NRBCs in Group-B was 5.41 ± 3.91. The difference was statistically significant. The mean cord blood NRBCs and mean maternal NRBCs in mothers with severe pre-eclampsia was significantly higher as compared to women in mild pre-eclampsia. In conclusion fetal response to utero–placental insufficiency in pre-eclampsia leads to elevated NRBC in the cord blood. The positive correlation between maternal and cord blood NRBC counts in pre-eclamptic patients indicates that maybe the hypo perfused placenta plays a role in the correlated alteration of the maternal and fetal NRBC count.
Keywords: NRBC, pre-eclampsia, hypoxia.

INTRODUCTION

Pre-eclampsia is a multisystem disorder of unknown etiology characterized by development of hypertension to the extent of 140/90 mm of Hg or more with proteinuria after the 20[th] week of pregnancy in previously normotensive and non-proteinuric women. Pre-eclampsia is strongly associated with adverse pregnancy outcome. It is a leading cause of maternal and fetal morbidity and mortality throughout the world and complicates an estimated 6–8% of pregnancies[1].

Nucleated red blood cells (NRBCs) are actually precursors for production of normal erythrocytes. They are primarily produced in the fetal bone marrow in response to erythropoietin and are stored in the marrow as precursors to reticulocytes and mature erythrocytes. As erythropoietin does not cross the placenta, elevated erythropoietin concentrations in fetal cord blood in cases of hypoxemia are of fetal origin. Many acute and chronic stimuli causes increase in circulating NRBCs from either increased erythropoietic activity or a sudden release from the marrow storage pools. Increase of NRBC counts in fetal hypoxia brought out the consideration of using the NRBC counts as a marker for hypoxia and possible predictor of adverse outcome of affected newborn.

Pre-eclampsia is considered to be a state of deterioration of utero–placental perfusion. This condition is associated with inadequate blood supply to the fetus, which can result in chronic hypoxia, as a result it enhances the production of NRBC in the fetus.[2] Therefore this study was conducted to investigate the differences in maternal and cord blood NRBC counts between pre-eclamptic and healthy parturients and to determine the correlation between the NRBC counts of cord and maternal blood with severity of pre-eclampsia.

METHODS

The present study was done to evaluate the influence of pre- eclampsia on nucleated RBCs in maternal and cord blood. It was a hospital based observational study, done in the Department of Obstetrics & Gynaecology, S.M.S. Medical College, and Jaipur from Feb 2013 to July 2013. The sample size was calculated at 95% confidence interval, at 80% study

power and α error 0.05. 120 women with pre-eclampsia were included in the study group (Group A) and 120 normotensive women in control group (Group B) on first come first basis in this study after applying inclusion and exclusion criteria and obtaining informed written consent.

Inclusion Criteria: Singleton, term pregnancy

Exclusion Criteria: Multi fetal pregnancy, Intrauterine fetal demise, congenital malformation, pre existing hypertensive, cardiovascular or renal disease, diabetes mellitus or chronic disease, maternal smoking, difficult delivery

Immediately after delivery of the fetus the umbilical cord was double-clamped and 1 mL umbilical cord blood was collected in a tube containing 1.5 mg ethylene diamine tetra-acetic acid (EDTA). 1 mL of maternal venous blood was collected in the same manner simultaneously. A complete blood count was performed using an automated cell counter. Blood films were prepared and stained using the leishman stain for 20 min. The number of NRBC per 100 leukocytes was counted. All data were entered on MS excel sheet and the data were analyzed. Quantitative data were summarized in form of mean and S.D. (Standard Deviation) and the difference in means were analyzed in using student't' test. The level of significance for all statistical analysis was kept at <0.05.

RESULTS

The mean age of the women was 23.46 ± 4.24 yrs in Group-A (pre-eclampsia) and 24.03 ± 4.79 yrs in Group-B (normotensive). 58.33% of women in Group-A and 60.83% of women in Group-B belonged to urban population. Overall out of 240 participants 60% of women resided in urban areas where as 40% of women resided in rural areas. 45.83% of women in Group-A and 41.67% of women in Group-B were illiterate. 44% of women attending the study were illiterate. Majority of the women in both the groups were Hindus. 75% in Group-A (pre-eclampsia) and 76.67% in Group-B (normotensive) (Table-1). This shows that study and control groups are comparable with respect to the profile of the participants.

The mean Maternal NRBCs/100 WBCs was 5.85 ± 4.022 in Group-A (pre-eclampsia) as compared to 2.33 ± 2.571 in Group-B (normotensive), which was statistically significant (Table-2). The mean cord blood NRBCs in Group-A (pre-eclamptic) was 16.19 ± 7.052 and mean cord blood NRBCs in (normotensive) Group-B was 5.41 ± 3.91. The difference was statistically significant (Table-3). The mean cord blood NRBCs (20.29 ± 5.41) in mothers with severe pre-eclampsia was significantly higher as compared to women in mild pre-eclampsia (13.73 ± 6.80) (Table-4). The difference in mean maternal NRBCs in cases of severe pre-eclampsia (8.62 ± 3.23) was statistically significant as compared to women with mild pre-eclampsia (4.19 ± 3.51). (Table-5).

Table – 1: Distribution of Cases According to Various Parameters

	Group A	**Group B**	**P-value, LS**
Age	23.46 ± 4.24 yrs	24.03 ± 4.79 yrs	< 0.55, NS
Residence			
Urban	70	73	
Rural	50	47	= 0.792, NS
Literacy			
Illiterate	55	50	0.603, NS
Literate	65	70	
Religion			
Hindu	90	92	0.361, NS
Muslim	30	28	

Table – 2: Distribution of Cases According to Maternal NRBCs / 100 WBCs

Groups	**No.**	**Mean**	**P Value, LS**
Group-A	120	5.85 ± 4.022	<0.001, Sig
Group-B	120	2.33 ± 2.571	
Total	**240**	**4.09 ± 3.803**	

Table – 3: Distribution of Cases According to Cord Blood NRBCs / 100 WBCs

Groups	**No.**	**Mean**	**P Value, LS**
Group-A	120	16.19 ± 7.052	<0.001, Sig
Group-B	120	5.41 ± 3.91	
Total	**240**	**10.8 ± 7.846**	

Table – 4: Association of Severity of Pre-eclampsia with Cord Blood Nucleated Count

Severity of Pre-eclampsia	No.	Mean	P Value, LS
Mild	75	13.73 ± 6.80	<0.001, Sig
Severe	45	20.29 ± 5.41	
Total	**120**	**16.19 ± 7.05**	

Table – 5: Association of Severity of Pre-eclampsia with Maternal NRBCs / 100 WBCs

Severity of Pre-eclampsia	No.	Mean	P Value, LS
Mild	75	4.19 ± 3.51	<0.001, Sig
Severe	45	8.62 ± 3.23	
Total	**120**	**5.85 ± 4.02**	

DISCUSSION

Pre-eclampsia is characterized by endothelial damage, platelet activation and intravascular coagulation that may lead to utero placental insufficiency. It has been suggested that a compensatory fetal response to this utero placental insufficiency in pre eclampsia occurs in the form of increased erythropoiesis and increase in the number of erythroblasts, and trafficking of fetal cells into maternal periphery is disturbed in pre eclampsia which can result in elevation of NRBCs in maternal blood.

Mean age of women was 23.46 ± 4.24 yrs in Group-A (pre-eclampsia) and 24.03 ± 4.79 yrs in Group-B (normotensive). Our findings are in concurrence with earlier studies conducted by different authors. BS Aali *et al.;* [3] in their study found the mean age of the normotensive women was 25.4 ± 5.1 yrs whereas in study group it was 27.2 ± 6.3 yrs respectively The difference was statistically not significant (P = 0.070). In the study of S Sivakumar *et al.; [4]*, the mean age was 23.38 yrs in normotensive women and 24.3 yrs in the pre-eclamptic women that was not statistically significant. The mean age was slightly more in the study of Shripad Hebbar *et al.;* [5] (27.3 ± 3.8 yrs in control group, 26.8 ± 4.5 yrs in pre-eclampsia group).

The mean maternal NRBCs / 100 WBCs was 5.85 ± 4.022 in Group-A as compared to 2.33 ± 2.571 in Group-B and the difference was statistically significant (P < 0.001). Our findings are in agreement with the study of Davari Tanha F6, The maternal NRBC count was significantly higher in the pre-eclampsia group than in the normotensive group (2.64 ± 1.23 v/s 0.44 ± 0.55). In the study of Shripad Hebbar *et al.;* [5] and BS Aali *et al.;* [3] maternal NRBC count in Pre-eclampsia Group was higher than in normotensive group (2.4 ± 9.0 v/s 0.8 ± 1.5 and 2.70 ± 13.10 v/s 1.45 ± 14.20 respectively) but the difference was statistically not significant in both the studies. It has been suggested recently that the trafficking of fetal cells into the maternal periphery is disturbed in women with pre-eclampsia, which can result in elevation of NRBC in the maternal blood.

The mean cord blood NRBCs in Group-A was 16.19 ± 7.052 and mean NRBCs in Group-B was 5.41 ± 3.91 which was statistically significant (P < 0.001). Our findings are in concurrence with earlier studies conducted at different places and reported by different investigators. The mean cord blood NRBC count in the control group was 6.2 ± 8.1 compared to 18.2 ± 31.8 in pre-eclamptic groups in the study of BS Aali *et al.;[3]*. S Sivakumar et al4, Shripad Hebbar *et al.;* [5] and Roya Faraji Darkhaneh *et al.;* [7] in their studies reported that mean cord blood NRBC s count in pre-eclamptic group was significantly higher compared to normotensive group,(7.38 v/s 1.72, 40.0 ± 85.1 v/s 5.9 ± 6.3 and 11.12 ± 5.5 v/s 2.74 ± 2.9 respectively. It has been stated that the inability of cyto tropho blasts to differentiate correctly and subsequent failure to invade the uterus and its arterioles efficiently in pre-eclampsia lead to a relatively hypoxic placenta. So compensatory mechanisms like enhanced production of nucleated RBCs are activated to counteract this imbalance. Thus increased NRBCs counts are seen in cord blood of pre-eclamtic mothers.

The mean cord blood NRBCs in women with mild pre-eclampsia was 13.73 ± 6.80 and in women with severe pre-eclampsia was 20.29 ± 5.41 which was statistically significant (P < 0.001). Maha M AL Bayati *et al.; [8]* found that mean cord blood NRBCs were 8.67 ± 7.49 in women with mild pre-eclampsia and 12.44 ± 8.25 in women with severe pre-eclampsia, which was statistically insignificant (P < 0.11). BS Aali *et al.;* [3] found no significant relationship between severity of pre-eclampsia and the NRBC count. The increased number of cord blood NRBCs in severe pre-eclampsia in our table can be explained due to the fact that increase in severity of intrauterine hypoxia leads to more production of erythroblasts.

The mean maternal NRBCs in mild pre-eclampsia were 4.19 ± 3.51 and in severe pre-eclampsia were 8.62 ± 3.23, which was statistically significant (P < 0.001). Maha M AL Bayati *et al.;* found that maternal NRBCs in mild pre- eclampsia was 3.89 ± 6.16 and in

severe pre-eclampsia was 4.53 ± 9.19, which was statistically insignificant.

CONCLUSION

Considering the fact that NRBC count increases in maternal and cord blood in women with pre-eclampsia, NRBCs level in maternal and cord blood is a probable investigative parameter to fulfill the search for a marker of hypoxia that is highly specific and at the same time easily accessible and universally available even at peripheral centres. Additional research will also be required to investigate whether abnormal fetal cell traffic of NRBC may be detectable even before the development of the clinical signs of pre-eclampsia. The presence of fetal erythroblasts in maternal blood, in combination with other biochemical markers, would be useful in screening for pre-eclampsia

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