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Cord Blood Total WBC Count and Neutrophil Count Changes in Newborn of Preeclamptic Mother

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Abstract

Introduction: Preeclampsia is a hypertensive disorder during pregnancy which may severely impact the health of mothers and their newborns. The newborn of preeclamptic mother should be carefully monitored and managed for the purpose of reducing perinatal mortality and morbidity. ***Aim of the Study:*** The aim of this study was to evaluate the changes in cord blood total count of WBC and absolute neutrophil count in newborn of preeclamptic mother. ***Methods:*** This cross-sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka, Bangladesh from January 2017 to December 2017. Total 60 newborns were included in this study. The subjects were divided into 2 groups. Group A (Study group): Thirty (30) newborns of preeclamptic mother and Group B (Control group): Thirty (30) newborns of healthy pregnant mother. The subjects were selected from Department of Obstetrics and Gynecology, Dhaka Medical College Hospital, Dhaka on the basis of exclusion and inclusion criteria. Five (5) ml. of cord blood from each newborn was collected in EDTA tube after delivery and haematological test for total WBC count and absolute neutrophil count was done. These parameters were estimated in the Department of Hematology, Dhaka Medical College Hospital, Dhaka. Data were collected in pre-designed structured questionnaire form by the researcher herself. For statistical analysis Unpaired Student's "t" test, Chi Square test and Pearson's correlation coefficient (r) test were performed as applicable using SPSS for windows version 16.0. *p* value <0.05 was accepted as level of significance. ***Results:*** In this study, the mean (±SD) maternal systolic blood pressure of the study group A and control group B were 173.00 ± 19.73 and 114.83 ± 11.72 mm Hg respectively. In this study, the mean (±SD) maternal systolic blood pressure was significantly (p<0.001) higher in group A in compared to group B. The mean (±SD) maternal diastolic blood pressure of the study group A and control group B were 108.33 ± 9.52 and 73.33 ± 9.07 mm Hg respectively. In this study, the mean (±SD) maternal diastolic pressure was significantly (*p*<0.001) higher in group A in comparison to that of group B. The mean (± SD) total count of WBC was 9.62 ± 1.86 × 10^3/µl and 17.38 ± 3.31 × 10^3/µl in group A and B respectively. In this study, the mean (±SD) total count of WBC was lower in group A in comparison to that of group B which was statistically significant (*p*<0.001). In this study, mean (±SD) Absolute Neutrophil Count (ANC) was 5.76±2.01 ×10^3/µl and 10.45±1.90 ×10^3/µl in group A and B respectively. In this study, the mean (±SD) absolute neutrophil count was lower in group A in comparison to that of group B which was statistically significant (*p*<0.001). Maternal systolic blood pressure showed negative correlation (- 0.953) with total count of WBC in newborn of preeclamptic mother, which was statistically significant (*p*<0.001). Maternal diastolic blood pressure showed negative correlation (-0.957) with total WBC count in newborn of preeclamptic mother, which was statistically significant (*p*<0.001). Maternal systolic blood pressure showed negative correlation (- 0.951) with absolute neutrophil count in newborn of preeclamptic mother, which was statistically significant (*p*<0.001). Maternal diastolic blood pressure showed negative correlation (-0.953) with absolute neutrophil count in newborn of preeclamptic mother, which was statistically significant (*p*<0.001). ***Conclusion:*** The total WBC count and absolute neutrophil count in the cord blood of the newborn of preeclamptic mother were lower than those of healthy pregnant mother, but they were within the normal range, it can be inferred after studying the study's findings. These changes were significantly related to severity of maternal blood pressure.

Keywords: Cord Blood, Total WBC Count, Absolute Neutrophil Count, Newborn of Preeclamptic Mother.

I. INTRODUCTION

Preeclampsia (PE) is a multisystem disorder that affects specifically the pregnant women and is responsible for various maternal and neonatal complications. Preeclampsia is defined as elevated level of blood pressure≥140/90 mmHg and high protein levels in the urine ≥300 mg/24 hour after 20 weeks of gestation in a pregnant woman who had no history of hypertension [1]. The onset of this condition may be linked to changes in the lipid profile, leukocyte

activation, increased inflammatory response, and oxidative stress in the maternal circulation [2-5]. An inflammatory reaction is often accompanied by rising levels of acute-phase proteins, proinflammatory cytokines, and leukocyte activity [6]. Inflammation is often accompanied by an increase in the number of circulating leukocytes and the contact between leukocytes and endothelial cells depends on cell adhesion molecules (CAM). Nearly all leukocytes express the glycoprotein L-Selectin, which is necessary for leukocyte adherence to the endothelium and blood vessel rolling [7]. Several cytokines, such as TNF, as well as some chemoattractants generated during an inflammatory phase may cause neutrophil activation. The metabolic activation of neutrophils and the release of their granules into the blood and tissues during this process help to increase the inflammatory response and/or oxidative stress [8]. A glycoprotein called lactoferrin is stored in the specialized or secondary granules of neutrophils. It plays a role in the control of the immune response and has antibacterial and anti-inflammatory properties [9]. The protective effects of lactoferrin are brought on by a decrease in the production of TNF and IL-6, two pro-inflammatory cytokines [10]. The leucocytes, mobile units of body's protective system are classified into granulocytes (neutrophils, eosinophils, basophils) and agranulocytes (monocytes and lymphocytes). They are formed in the bone marrow (granulocytes and monocytes and few lymphocytes) and partially in the lymphoid tissue (lymphocytes and plasma cells). Blood cells are originated in the bone marrow from multipotent hematopoietic stem cell. The multipotent stem cell reproduces into committed stem cells for specific blood cell type. There are different growth factors that regulate the clonal maturation of committed cells to produce different types of blood cells [11]. The bone marrow is the site of neutrophil production and the process is regulated by cytokine- granulocyte colony stimulating factor (G- CSF) [12]. The newborns of preeclamptic mothers have an increased risk for development of neonatal neutropenia specially in premature newborns. So, the affected newborns are more vulnerable for localized and systemic infections and sepsis [13]. Koenig and Christensen [14] suggested that this type of neutropenia may be due to decrease in growth factor which increase the neutrophil production or due to decrease in response of progenitors to growth factor or due to presence of inhibitor of neutrophil production. In some studies, total white blood cell (WBC), leukocytes count and absolute neutrophil count were significantly decreased in newborn of preeclamptic mother [15, 16]. Again, Sivakumar *et al.*, [17] found no significant change of neutrophil count between newborns of preeclamptic mother and healthy pregnant mother. Neonatal thrombocytopenia was observed in 47% newborn of preeclamptic mother which led to serious complications like sepsis and bleeding tendencies including intracranial hemorrhage [18]. Several studies have been done around the world to observe the effects of preeclampsia on newborn blood parameters. As, there is less published data available regarding this topic in Bangladesh, the effect of preeclampsia on the blood parameters of newborn is not precisely known. Thus, this current study was conducted to evaluate the changes in cord blood total count of WBC and absolute neutrophil count in newborn of preeclamptic mother.

II. OBJECTIVES

To evaluate the changes in cord blood total count of WBC and absolute neutrophil count in newborn of preeclamptic mother.

III. METHODOLOGY & MATERIALS

This cross-sectional study was conducted in Department of Physiology, Dhaka Medical College, Dhaka, Bangladesh during the period from January 2017 to December 2017. Total 60 newborns were included in this study. The subjects were divided into 2 groups. Group A (Study group): Consisted of thirty (30) newborns of preeclamptic mother and Group B (Control group): Consisted of thirty (30) newborns of healthy pregnant mother. After selection of the subjects, the nature, purpose and benefit of the study were explained to the pregnant women and their parents or legal guardians in details and informed written consent was taken from the pregnant women, their parents/legal guardians. The research work was carried out after obtaining ethical clearance from concerned Departments, Research Review Committee and Ethical Review Committee of Dhaka Medical College, Dhaka. Before taking blood, detailed personal history, family history and medical history with onset of symptoms, blood pressure recording and presence of seizures of the pregnant women were noted. Urine sample (10ml) was collected in a plain and dry glass test tube for urinary dipstick test. With all aseptic precaution after delivery of newborn 5 ml cord blood was collected by a 10-cc disposable plastic syringe in a tube containing 1.5 mg EDTA from each newborn. Then blood samples were sent for hematological analysis in the Department of Hematology, Dhaka Medical College Hospital, Dhaka. Collected blood samples were analyzed by Automated Hematology Analyzer (Sysmex XT-2000). Details of the labor including mode of delivery, duration of labor, rupture of membrane and presence of any complications during labor were recorded. Neonatal data such as sex, date of delivery, time of birth, Apgar scores at 1^{st} and 5^{th} min, birth weight were recorded in prefixed questionnaire. Complete blood counts were estimated in Department of Hematology, Dhaka Medical College Hospital, Dhaka. All the parameters were expressed as mean and standard deviation (mean ± SD). Unpaired Student's 't' test was performed to compare all the quantitative parameters between the two groups. Chi Square test was performed to the qualitative parameters between the groups. Pearson's correlation co-efficient (r) test was performed to observe the relationship of hematological changes of newborn of preeclamptic

mother. *p* value <0.05 was accepted as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (statistical package for social sciences) version 16.0.

Inclusion Criteria For both groups:

1. Newborn of both sexes within one hour of delivery.

Inclusion criteria for Group A:

1. Newborn of mother diagnosed as preeclampsia [8].

Inclusion criteria for Group B:

1. Newborn of healthy pregnant mother.

Exclusion Criteria for both groups:

1. Newborn of mother with pre-existing hypertension, diabetes mellitus, severe anemia, heart disease, liver disease, kidney disease, Rh incompatibility and ABO incompatibility.
2. Newborn of mother with habit of smoking, premature rupture of membrane.
3. Newborn of mother with history of taking drug like aspirin.
4. Newborn with chromosomal anomaly, congenital malformation.

IV. RESULTS

A total number of 60 newborns were selected for this study. Among them, 30 newborns of preeclamptic mother were selected as study group (Group A) and 30 sex matched newborns of healthy mother were selected as control (Group B) for comparison. Table I demonstrates the general characteristics of the subjects in both groups. In this study, the maternal age range of the study population was between 15-40 years. The mean (±SD) maternal age of study group A and control group B were 24.12 ± 5.49 and 24.00 ± 4.83 years respectively. No statistical difference was observed between these two groups. So, maternal age was matched between two groups. In this study, there were 19 primi and 11 multi para pregnant women in study group A and 18 primi and 12 muti para pregnant women in control group B. No statistical difference was observed between these two groups. So, maternal parity was matched between two groups. The mean (± SD) gestational age (weeks) was 35.70 ± 2.28 and 38.03± 1.22 weeks in study group A and control group B respectively. In this study, the mean (±SD) gestational age (weeks) was significantly (p<0.001) lower in group A in comparison to that of group B. In the study group A, 15(50%) newborns were male and 15(50%) newborns were female. In the control group B, 15 (50%) newborns were male and 15(50%) newborns were female. No statistical difference was observed between these two groups. Therefore, newborns of both the groups were matched for sex. In this study, the mean (± SD) Apgar score in 1st minute in study group A and control group B were 6.07±0.89 and 7.6 ±0.49 respectively. In this study, the mean (± SD) Apgar score in 5 th minute in study group A and control group B were 8.03 ±0.87 and 9.47 ±0.62. Both Apgar score in 1st minute and in 5th minute were significantly (p<0.001 and p<0.001) lower in study group A compared to control group B. The mean (±SD) maternal systolic blood pressure of the study group A and control group B were 173.00 ± 19.73 and 114.83 ± 11.72 mm Hg respectively. In this study, the mean (±SD) maternal systolic blood pressure was significantly (p<0.001) higher in group A in comparison to that of group B. The mean (±SD) maternal diastolic blood pressure of the study group A and control group B were 108.33 ± 9.52 and 73.33 ± 9.07 mm Hg respectively. In this study, the mean (±SD) maternal diastolic pressure was significantly (p<0.001) higher in group A in comparison to that of group B. Table II and figure 1 demonstrates that the mean (± SD) total count of WBC was 9.62 ± 1.86 × 10^3/µl and 17.38 ± 3.31 × 10^3/µl in group A and B respectively. In this study, the mean (±SD) total WBC count was lower in group A in comparison to that of group B which was statistically significant (p<0.001). Table II and Figure 2 demonstrates that the mean (±SD) Absolute Neutrophil Count (ANC) was 5.76±2.01 ×10^3/µl and 10.45±1.90 ×10^3/µl in group A and B respectively. In this study, the mean (±SD) absolute neutrophil count was lower in group A in comparison to that of group B which was statistically significant (p<0.001). Table III and Figure 3 shows the correlation of total count of WBC with maternal systolic and diastolic blood pressure in study group. Maternal systolic blood pressure showed negative correlation (- 0.953) with total WBC count in newborn of preeclamptic mother, which was statistically significant (p<0.001). Maternal diastolic blood pressure showed negative correlation (-0.957) with total WBC count in newborn of preeclamptic mother, which was statistically significant (p<0.001). Table III and Figure 4 demonstrates the correlation of absolute neutrophil count with systolic and diastolic blood pressure in study group. Maternal systolic blood pressure showed negative correlation (-0.951) with absolute neutrophil count in newborn of preeclamptic mother, which was statistically significant (p<0.001). Maternal diastolic blood pressure showed negative correlation (-0.953) with absolute neutrophil count in newborn of preeclamptic mother, which was statistically significant (p<0.001).

Table-I: General characteristics of the subjects in both groups (N=60)

Parameters		Group-A	Group-B	*p* value
		Newborns of preeclamptic mother (n=30)	Newborns of healthy mother (n=30)	
Maternal age (years) [a]	Mean ± SD	24.12 ± 5.49	24.00 ± 4.83	0.929[ns]
Para[b]	Primi	19 (63.3%)	18 (60%)	0.791[ns]
	Multi	11 (36.7%)	12 (40%)	
Gestational age (weeks) [a]	Mean ± SD	35.70 ± 2.28	38.03 ± 1.22	<0.001[***]
Sex of newborn (%) [b]	Male	15 (50%)	15 (50%)	1.000[ns]
	Female	15 (50%)	15 (50%)	
Apgar score (At the first minute) [a]	Mean ± SD	6.07 ± 0.89	7.60 ± 0.49	<0.001[***]
Apgar score (At the fifth minutes) [a]	Mean ± SD	8.03 ± 0.87	9.47 ± 0.62	<0.001[***]
Systolic BP of mother [a] (mmHg)	Mean ± SD	173 ± 19.73	114.83 ± 11.72	<0.001[***]
Diastolic BP of mother [a] (mmHg)	Mean ± SD	108.33 ± 9.52	73.33 ± 9.07	<0.001[***]

a=Unpaired Student's 't' test; b=Chi Square test; The test of significance was calculated and *p* value < 0.05 was accepted as level of significance; N= total number of subjects, n = number of subjects in each group; ***= highly significant; ns=not significant

Table-II: Study parameter of the subjects in both groups (N=60)

Parameters	Group-A	Group-B	*p value*
	Newborns of preeclamptic mother (n=30)	Newborns of healthy mother (n=30)	
WBC count ($\times 10^3/\mu l$) [a]	9.62 ± 1.86	17.38 ± 3.31	<0.001[***]
ANC ($\times 10^3/\mu l$) [a]	5.76±2.01	10.43±1.90	<0.001[***]

Results were expressed as mean ± SD; a=Unpaired Student's 't' test; b=Chi Square test; The test of significance was calculated and *p* value < 0.05 was accepted as level of significance; N= total number of subjects, n = number of subjects in each group; ***= highly significant; *= significant; ns= not significant

Table-III: Correlation of maternal blood pressure with study parameters in study group (n=30)

Study parameters	Systolic blood pressure		Diastolic blood pressure	
	r	*p*	r	*p*
WBC count ($\times 10^3/\mu l$) [a]	− 0.953	<0.001***	− 0.957	<0.001[***]
ANC ($\times 10^3/\mu l$) [a]	− 0.951	<0.001***	− 0.953	<0.001[***]

Pearson's correlation coefficient (r) test was performed to observed relationship between maternal blood pressure with different study parameters. The test of significance was calculated and *p* value < 0.05 was accepted as level of significance; a=Unpaired Student's 't' test; n = number of subjects in study group; ***= highly significant; *= significant; ns= not significant

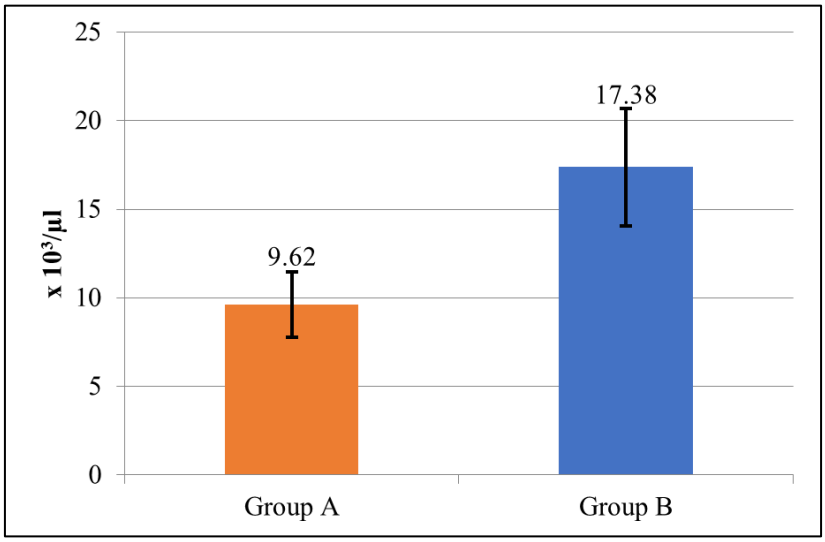

Figure 1: Mean total count of WBC in both groups (N=60)

Group A: Newborns of preeclamptic mother; Group B: Newborns of healthy mother; N= total number of subjects; WBC= White blood cell

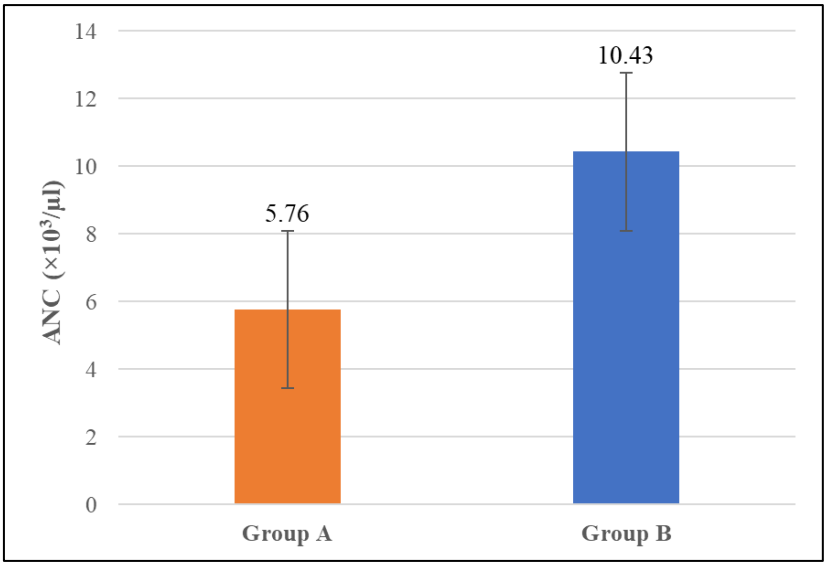

Figure 2: Mean absolute neutrophil count in both groups (N=60)

Group A: Newborns of preeclamptic mother; Group B: Newborns of healthy mother; N= total number of subjects

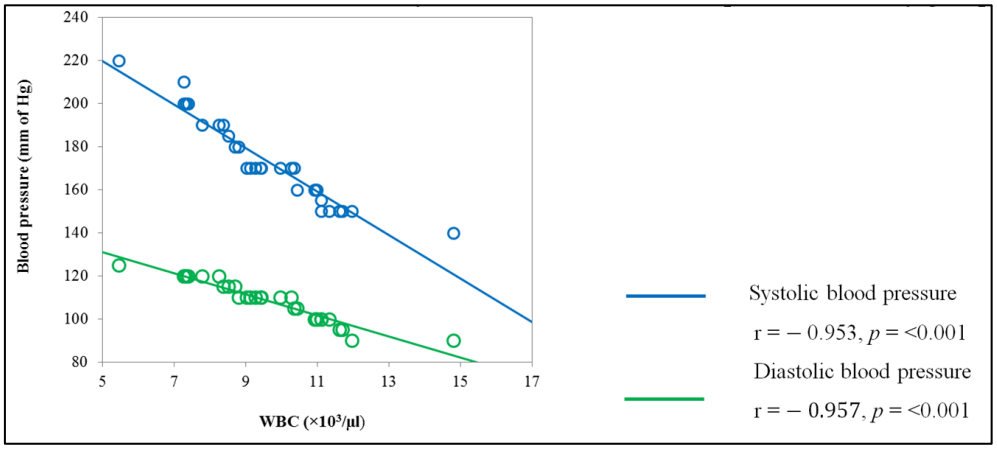

Figure 3: Correlation of total count of WBC with systolic and diastolic blood pressure in study group (n=30)

n = number of subjects in study group; Study subjects: Newborns of preeclamptic mother

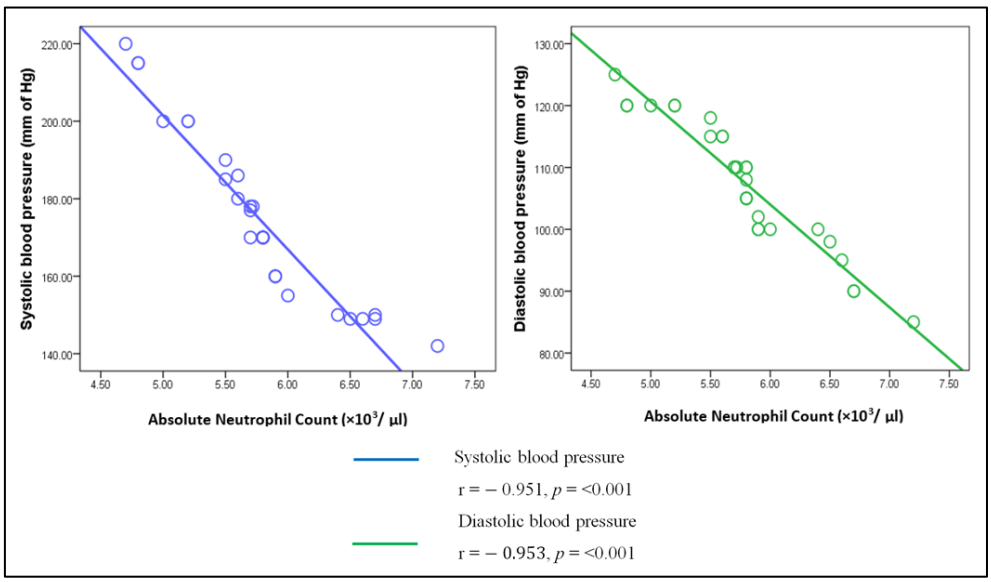

Figure 4: Correlation of absolute neutrophil count with systolic and diastolic blood pressure in study group (n=30)

n = number of subjects in study group; Study subjects: Newborns of preeclamptic mother

V. DISCUSSION

In the present study, all the parameters in newborns of healthy pregnant women were within physiological limit. Almost similar types of findings were observed by various investigators from different countries [18-20]. In the present study, the maternal blood pressure was higher in group A than that of group B and the result was statistically significant ($p < 0.001$). This finding was in agreement with the study of many researchers of different countries [21-23]. In the present study, the mean WBC count were significantly ($p < 0.05$) lower in newborns of preeclamptic mothers than that of newborn of healthy pregnant mother. This finding was in agreement with the study of many researchers of different countries [15, 16, 20, 24]. On the contrary, Sivakumar *et al.,* [17] found no significant changes in WBC count in newborns of preeclamptic mothers than that of newborns of healthy pregnant mothers with its differentials. This disagreement in findings might have occurred due to different methodology used in that study. A prospective case-control study was done by Eman *et al.,* [18] on 155 neonates of mothers with pregnancy induced hypertension (PIH) in India. Their results showed that leukocyte indices (total count of WBC, absolute neutrophil count and absolute lymphocyte count) were significantly decreased in neonates born to PIH mother than the control group. They concluded that the hematological changes of newborn of PIH mother increase the risk of sepsis, bleeding tendency and mortality in the neonates. Mouna *et al.,* [24] conducted a prospective case control study in India on 60 neonates of women with preeclampsia. Their results showed significantly that leucocyte was significantly decreased in newborn of preeclamptic mother. They concluded that early hematological screening will be helpful for decreasing morbidity in newborn of mother with preeclampsia. In the present study, total count of WBC and absolute neutrophil count were lower which was most likely due to placental hypoxia. Hypoxia can be effectively used to describe oxygen states relative to some normative value, or alternatively, it can be restricted to describing a state that evokes specific cellular responses [25, 26].

In the present study, total count of WBC and absolute neutrophil count were lower in study group which was likely due to placental hypoxia induced by uteroplacental insufficiency caused by defective placentation in preeclampsia. Chronic hypoxia leads to increase erythropoietin synthesis and enhance erythropoiesis to meet up the imbalance of oxygen demand [20, 22, 27]. In the bone marrow, proliferation and differentiation of hematopoietic progenitor in different cell lines occurs under the influence of different growth factors. Hematopoietic cells simultaneously can express separate receptors for different growth factors. So, erythroid progenitors (BFU-E) and GM progenitors can response to both erythropoietin and colony stimulating factors (CSF) [28]. When specific growth factor is increased and binds with its specific receptor, the number and sensitivity of receptors to other growth factors in the cell membrane is decreased. Erythropoietin reduces the affinity of CSF receptor for its specific ligand or reduces the CSF receptors on cell surface [29]. Fetal hematopoietic progenitors are susceptible to erythropoietin induced down regulation of leukocytes production by reducing clonal maturation of CFU-GM or reducing differentiation of granulocytes within the GM colonies. So, diversion of multipotent progenitors into erythroid progenitors (BFU- E) occurs and increases erythropoiesis and may subsequently lead to leukopenia [14, 30]. Koenig and Christensen suggested that neutropenia was caused by a decrease in growth factors which increase neutrophil production, and decrease in response of progenitor cells to growth factors and presence of inhibitor substance inhibiting neutrophil production [31]. These investigators showed that the activity of colony stimulating factor decreased in the placenta of hypertensive mothers and found an inhibitor substance inhibiting neutrophil production in the placenta. However, decrease in the response of progenitor cells to growth factors could not be shown. In another study, Fas–Fas ligand interaction was reported to be involved in leucopenia in preeclampsia [32]. In our study, total counts of leukocytes, neutrophils, lymphocytes, monocytes, and eosinophils were found to be significantly lower in the hypertensive group. These findings are thought to be caused by one or more of the aforementioned mechanisms.

Limitations of the Study

Although optimal care had been tried by the researcher in every step of the study, but there were some limitations. Evaluation of hematological parameters in preeclamptic mothers was not done financial constraints.

VII. CONCLUSION AND RECOMMENDATIONS

Total count of WBC and absolute neutrophil count in cord blood of newborn of preeclamptic mother were much lower than those of a healthy pregnant mother, but they were within the normal range, it can be inferred after analyzing the study's findings. These adjustments had a big impact how high the mother's blood pressure was. These changes should be kept in mind for the purpose of early hematological screening of cord blood in newborn of mother with preeclampsia. This may be helpful for early diagnosis and timely management of the related complications like infection and sepsis of these newborns. Evaluation of hematological parameters in preeclamptic mothers might be done to compare with the hematological alterations of the infant in order to get more conclusive results.

Conflict of Interest: None.

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