The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90 (2), Page 2170-2177

# A New Predictor for Growth Restriction in Preeclampsia. A Case Control Study

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## ABSTRACT

**Background:** Preeclampsia(PE) is culpable of the placental hypoxia that persists during pregnancy. The number of nucleated red blood cells in the cord blood (cNRBCs) is a sign of a hypoxic fetal environment. It might be a potential indication of intra-uterine growth restriction (IUGR).

**Objective:** The goal is to ascertain whether pre-eclampsia is related to an increase in the number of cNRBCs in cord blood, especially those with restricted growth.

**Methods:** This case control study was conducted on 150 neonates who were divided into three equal groups; group I included newborns of PE women, without IUGR, group II included newborns of PE women, with IUGR and group III included apparently healthy newborns of healthy non-PE pregnant women as a control group. As soon as the cord was clamped, samples for complete blood count and blood gases were taken from the umbilical vein.

**Results:** cNRBCs count was significantly higher in group with PE and IUGR compared to PE without IUGR and the control groups. The cutoff value of cNRBC to discriminate newborns of healthy mothers and those with PE was ≥ 8 cNRBCs/100 WBCs. Yet the value to discriminate newborns of PE mothers with IUGR and without IUGR was ≥ 22 NRBCs/100 WBCs.

**Conclusion:** When PE was compared to controls, it was discovered that cNRBCs were considerably greater. Moreover, higher cNRBCs was found in PE with IUGR compared to PE without IUGR. Thus, cNRBCs count has predictive value for IUGR. It may be used to tell growth-restricted babies from small-for-their-age children.

**Keywords:** preeclampsia, umbilical cord, nucleated red blood cell count, intrauterine growth restriction.

## INTRODUCTION

Pre-eclampsia (PE), a condition that impacts 5-8% of pregnancies, significantly increases mother and infant morbidity and mortality worldwide [(1)].

Abnormal shallow trophoblast invasion of the mother's uterine spiral arteries has been linked to the development of PE [(2)]. Due to the decreased blood supply to the utero-placental bed as a result, placental hypoxia persists throughout pregnancy [(3)].

A large number of anti-angiogenic chemicals are secreted by the placenta in response to this hypoxic situation, which results in significant endothelial dysfunction and the pre-eclampsia clinical symptoms [(4)].

Pre-eclampsia (PE) is a condition that only occurs during pregnancy and is characterized by proteinuria and hypertension. It commonly appears after 20 weeks of pregnancy [(5)].

When a newborn weighs less than the 10th percentile for gestational age, it is diagnosed as IUGR (intra uterine growth restriction) [(6)]. Particularly in those who are born very preterm, newborns with IUGR are more likely to experience higher morbidity and mortality, particularly if they were preterms. Numerous long-term impacts have been identified by studies, ranging from normal to minor IQ reductions to a noticeably increased risk of cerebral palsy [(7)].

Nucleated red blood cells (NRBCs), are present in fetal bone marrow, and they can be released in the neonatal circulation. Erythropoietin is primarily responsible for their creation [(8)].

Increased erythropoietic activity or a rapid release from the marrow storage pools were two of the many acute and chronic factors that caused an increase in the amount of circulating NRBCs. It seems to be one of the most dependable indicators of a hypoxic perinatal environment [(9)].

## PATIENTS AND METHODS

### Study design:

Our case control study was carried out in a period of 10 months in the Obstetrics and Gynaecology Hospital, Ain Shams University.

The studied participants were split into three groups; group I included 50 newborns of pre-eclamptic women, without IUGR, group II included 50 newborns of pre-eclamptic women, with IUGR and group III included 50 apparently healthy newborns of healthy normotensive pregnant women as control.

After 20 weeks of gestation, pre-eclampsia was clinically defined as the de novo start of hypertension (systolic blood pressure 140 mmHg or diastolic blood pressure 90 mmHg) and proteinuria (300 mg/24 h) [(5)].

Neonates born to women with autoimmune disorders, diabetes, chronic hypertension, cardiovascular, renal, or hepatic diseases were excluded. Additionally, those neonates with RH iso-immunization,



Received: 18/09/2022

Accepted: 20/11/2022

congenital abnormalities, congenital infections, prolonged premature rupture of membranes lasting longer than 18 hours, chorioamnionitis, acute intrapartum hypoxia, or multiple gestations were also excluded.

For all enrolled newborns, detailed perinatal history taking was done. They were all examined thoroughly, and weighed in grams. APGAR score was recorded as well.

IUGR was defined as birth weight less than the 10th percentile for gestational age [6].

**Methodology:**

- Blood samples were obtained from the umbilical vein immediately following the clamping of the cord. CBC sample was collected on K3-EDTA and sent to the ASU laboratory where they were subjected to Abbott CELL-DYN 1800 analysis, blood smear preparation, and Leishman staining, followed by microscope visualization.
- A complete blood cell count was performed and the total white blood cell (WBC) count was determined.
- NRBCs was counted per 100 WBCs under microscope, then corrected WBCs count was calculated using the following formula:

$$\text{Corrected WBC count} = \frac{(\text{Uncorrected WBC count} \times 100)}{(\text{NRBC per 100 leucocytes} + 100)}$$

- Umbilical cord PH was determined. Blood gases sample withdrawn using heparinized syringes, and measured right away using the ABL800 FLEX blood gas analyzer.

**Ethical consideration:**

**The study protocol gained approval from the local Ethics Committee of the Pediatric Department, Faculty of Medicine, Ain Shams University. This work has been performed in agreement with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

***Statistical analysis***

The data was gathered, collated, and examined using the proper statistical methodologies before being used to create the demonstrative figures. Data analysis was done using IBM SPSS statistics (V. 22.0, IBM Corp., USA, 2013). In addition to median percentiles for quantitative non-parametric measurements, number and percentage were used to convey categorical data, as well as Mean ± SD for quantitative parametric measures. For parametric data, the Student t test was used to compare the means of two independent groups. Wilcoxon Rank Sum test was used to compare two independent groups for non-parametric data. For non-parametric data, the ranked Spearman correlation test was performed to investigate the potential relationship between each pair of variables within each group. The chi-square test was used to examine the relationship between each of the two variables or to compare the two independent groups in relation to the categorized data. The chance of mistake was regarded as significant at 0.05, very significant at 0.01 and 0.001. To find the most sensitive and precise cutoff for each technique, the ROC was built. AUC can also be calculated to assess the greatest distinguishing indicators between the comparison groups.

**RESULTS**

This case control study was conducted on 150 neonates. We first compared the infants of PE mothers (n=100) and those to normotensive mothers (n=50) as regards their demographic data and laboratory results in table (1) and (2) correspondingly.

**Table 1: Demographic characteristics of study groups**

| | **PE** (n=100) | **Control (n=50)** | **P-value** |
|---|---|---|---|
| | **Mean±SD, Median(IQ), N(%)** | | |
| **GA** (weeks) | 34.131± 2.3302 | 38.88± 1.16 | < 0.001 |
| **Birth weight** (grams) | 1665 (1300 - 2000) | 3500 (3200 - 3682.5) | < 0.001 |
| **APGAR (1min)** | 6 (6 - 7) | 7 (7 - 7) | < 0.001 |
| **APGAR (5min)** | 8 (7 - 9) | 9 (9 - 9) | < 0.001 |
| **Gender:**<br>Male<br>Female | <br>54 (54%)<br>46 (46%) | <br>25 (50%)<br>25 (50%) | 0.643 |
| **Maternal age** (years) | 28.51 ±4.26 | 29.18 ± 4 | 0.347 |
| **Maternal SBP** (mmHg) | 163.9 ± 8.5156 | 116.2± 7.25 | < 0.001 |
| **Maternal DBP** (mmHg) | 103.6± 7.9798 | 74.2 ± 5.38 | < 0.001 |

GA: gestational age, SBP: systolic blood pressure, DBP: diastolic blood pressure

**Table 2: Comparison of laboratory data between the PE and control groups**

| | **PE** (n=100) | **Control** (n=50) | **P-value** |
|---|---|---|---|
| **TLC** ($x10^3/mm^3$) | 9.45 | 13.9 | < 0.001 |
| **Hb** (g/dl) | 17.789 ±2.3553 | 15.932 ±1.1307 | < 0.001 |
| **Plts** ($x10^3/mm^3$) | 174.5 | 279.5 | < 0.001 |
| **cNRBCs** /100 WBCs | 24 | 2 | < 0.001 |
| **pH of the cord blood** | 7.2241 ± 0.047337 | 7.3037 + 0.024873 | < 0.001 |

TLC: total leucocytic count, Hb: hemoglobin, plt: platlet count, cNRBCs: cord blood nucleated red blood cells.

The 150 enrolled neonates were split into three equal groups; group I included newborns of PE women, without IUGR, group II included newborns of PE women, with IUGR and group III included apparently healthy newborns of healthy non-PE pregnant women as a control group. Their demographic data were compared and shown in table (3) and their laboratory results in table (4).

**Table 3: Demographic data of all studied groups**

| **Descriptive data** | **PE without IUGR** | **PE with IUGR** | **Control** | **P1** | | **P2** | | **P3** | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **Statistical test** | **P (Sig.)** | **Statistical test** | **P (Sig.)** | **Statistical test** | **P (Sig.)** |
| | **Mean±SD, Median(IQ), N(%)** | | | | | | | | |
| **GA** (weeks) | 33.95 ± 2.36 | 34.31± 2.31 | 38.88± 1.16 | t = -0.775 | 0.44 | t = 13.257 | < 0.001 HS | t = 12.49 | < 0.001 HS |
| **Birth weight** (grams) | 2000 1687.5 - 2400) | 1325 (1100 - 1620) | 3500 (3200 - 3682.5) | Z = -6.142 | < 0.001 HS | Z = -8.278 | < 0.001 HS | Z = -8.623 | < 0.001 HS |
| **APGAR (1min)** | 7 (6 - 7) | 6 (5 - 6) | 7 (7 - 7) | Z = -2.952 | 0.003 HS | Z = -4.856 | < 0.001 HS | Z = -7.193 | < 0.001 HS |
| **APGAR (5min)** | 8 (8 - 9) | 7 (7 - 8) | 9 (9 - 9) | Z = -3.17 | 0.002 HS | Z = -4.391 | < 0.001 HS | Z = -6.36 | < 0.001 HS |
| **gender:** Male Female | 26 (52%) 24 (48%) | 28 (56%) 22 (44%) | 25 (50%) 25 (50%) | **$x^2$= 0.374** | | | 0.829 NS | | |
| **Maternal age** (years) | 28.52±4.30 | 28.5 ±4.27 | 29.18 ± 4 | t = 0.023 | 0.981 NS | t = 0.794 | 0.429 NS | t = 0.821 | 0.414 NS |
| **Maternal Systolic BP** (mmHg) | 159.8 ±7.14 | 168 ± 7.82 | 116.2± 7.25 | t = -5.474 | < 0.001 HS | t = -30.291 | < 0.001 HS | t = -34.33 | < 0.001 HS |
| **Maternal Diastolic BP** (mmHg) | 99.6 ±7.27 | 107.6± 6.57 | 74.2 ± 5.38 | t = -5.774 | < 0.001 HS | t = -19.854 | < 0.001 HS | t = -27.825 | < 0.001 HS |
| **P1: Comparison between PE without IUGR & PE with IUGR.** **P2: Comparison between PE without IUGR & Control.** **P3: Comparison between PE with IUGR & Control.** | | | | | | **t = Student T Test** z = **Wilcoxon Rank Sum Test** **$x^2$= Pearson Chi-Square** | | | |

GA: gestational age, SBP: systolic blood pressure, DBP: diastolic blood pressure, **Mean±SD:**for parametric data, **Median(IQ):**for nonparametric data.

**Table 4: Laboratory data of all studied groups**

| Descriptive data | PE without IUGR | PE with IUGR | Control | P1 | | P2 | | P3 | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean±SD, Median(IQ) | | | Statistical test | P (Sig) | Statistical test | P (Sig) | Statistical test | P (Sig) |
| **TLC** ($x10^3/mm^3$) | 10 (8.075 - 11.525) | 8.9 (6.35 - 11) | 13.9 (11.875 - 15.6) | Z = -2.113 | 0.035 S | Z = -6.016 | < 0.001 HS | Z = -7.436 | < 0.001 HS |
| **HB** (g/dl) | 17.452 ±2.5243 | 18.126 ±2.1457 | 15.932 ±1.1307 | t = -1.439 | 0.154 NS | t = -3.886 | < 0.001 HS | t = -6.396 | < 0.001 HS |
| **Plts** ($x10^3/mm^3$) | 199 (157.75 - 241.5) | 150 (115 - 200.5) | 279.5 (251.5 - 302) | z = -2.968 | 0.003 HS | z = -6.757 | < 0.001 HS | z = -7.187 | < 0.001 HS |
| **PH** | 7.25358 ± 0.031386 | 7.19462 ± 0.042055 | 7.3037 ± 0.024873 | t = 7.945 | < 0.001 HS | t = 8.85 | < 0.001 HS | t = 15.786 | < 0.001 HS |

**P1: Comparison between PE without IUGR & PE/IUGR.**
**P2: Comparison between PE without IUGR & Control.**
**P3: Comparison between PE with IUGR & Control.**

**t = Student T Test**
z = **Wilcoxon Rank Sum Test**
**Mean±SD** for parametric parameters-
**Median(IQ)** for nonparametric parameters

The number of cord nucleated red blood cells (cNRBCs)/100 white blood cells (WBCs) was tabulated and compared in the 3 groups table (5) followed by a correlation done between the cNRBCs count and the clinical parameters table (6) pursued by a correlation between the cNRBCs count and the laboratory data of the 3 groups (7).

**Table 5: cNRBCs count in all groups**

| | | cNRBCs count / 100 WBCs | | |
|---|---|---|---|---|
| | | **Median (IQ)** | **Min** | **Max** |
| **PE without IUGR** | | 16 (12 - 20.25) | 4 | 60 |
| **PE with IUGR** | | 39.5 (27.25 - 50) | 11 | 860 |
| **Control** | | 2 (1 - 4) | 0 | 15 |
| **P1** | **Statistical test** | z = -6.927 | | |
| | **P** | < 0.001 | | |
| **P2** | **Statistical test** | z = -8.18 | | |
| | **P** | < 0.001 | | |
| **P3** | **Statistical test** | z = -8.626 | | |
| | **P** | < 0.001 | | |

**P1: Comparison between PE without IUGR & PE with IUGR.**
**P2: Comparison between PE without IUGR & Control.**
**P3: Comparison between PE with IUGR & Control.**

z = **Wilcoxon Rank Sum Test**

**Table 6: Correlation between cNRBCs count and clinical parameters**

| | PE without IUGR | | PE with IUGR | | Control | |
|---|---|---|---|---|---|---|
| | **R** | **P** | **R** | **P** | **R** | **P** |
| **Gestational age** | -0.323 | 0.022 | -0.383 | 0.006 | 0.032 | 0.826 |
| **Birth weight** | -0.329 | 0.02 | -0.343 | 0.015 | -0.11 | 0.425 |
| **APGAR** (1min) | -0.165 | 0.254 | -0.512 | 0 | -0.259 | 0.07 |
| **APGAR** (5min) | -0.332 | 0.018 | -0.572 | 0 | -0.019 | 0.898 |
| **Head Circumference** | ---- | ---- | -0.371 | 0.008 | ---- | ---- |
| **Maternal age** | -0.021 | 0.884 | -0.102 | 0.48 | 0.113 | 0.436 |
| **Maternal SBP** | 0.099 | 0.493 | 0.117 | 0.417 | 0.109 | 0.452 |
| **Maternal DBP** | 0.112 | 0.439 | 0.111 | 0.444 | 0.082 | 0.57 |
| **Ranked Spearman Correlation Test** | | | | | | |

**Table 7: Correlation between cNRBCs count and laboratory results**

| | PE without IUGR | | PE with IUGR | | Control | |
|---|---|---|---|---|---|---|
| | **R** | **P** | **r** | **P** | **r** | **P** |
| **TLC** ($x10^3/mm^3$) | -0.16 | 0.267 | -0.455 | 0.001 | 0.061 | 0.675 |
| **HB** (g/dl) | 0.004 | 0.977 | 0.319 | 0.024 | 0.326 | 0.021 |
| **Plts** ($x10^3/mm^3$) | -0.148 | 0.304 | -0.245 | 0.086 | -0.103 | 0.477 |
| **PH** | -0.792 | 0 | -0.886 | 0 | -0.088 | 0.541 |
| **Ranked Spearman Correlation Test** | | | | | | |

## DISCUSSION

In our study, gestational age was comparable in the two groups of PE patients, with/without IUGR (34.31±2.31 & 33.95±2.36 respectively), which was significantly lower than controls (38.88± 1.16). This was in line with a study done by ***Catarino et al.*** that examined the amounts of oxidative stress and inflammatory markers in umbilical cord blood from normal and PE pregnancies and maternal blood, respectively. The findings demonstrated that, in comparison to normal instances, gestational age was substantially lower in PE cases [(10)].

In our study, the birth weight was substantially lower in PE with IUGR than PE without IUGR [1325 (1100-1620) & 2000 (1687.5-2400) respectively]. Compared to the control group, it was significantly lower in PE [3500 (3200-3682.5)]. This is coherent with the study by ***Groom et al.***, which described the relationship between small for gestational age (SGA) newborns and PE and tried to figure out how this relationship changed with delivery gestational age. 520 women in total got PE. Coexisting PE was more likely to happen in SGA infants delivered preterm than at term in women. Preterm PE women were more likely than term PE women to give birth to an SGA child [(11)].

In our study, the studied groups were comparable as regard to newborns sex. In line with this, ***Tokmak et al***., assessed the maternal anti-mullerian hormone's predictive significance in poor maternal and perinatal outcomes in preeclampsia. PE cases designated as study group (45 cases) and control group (42 instances) were assessed. In terms of birth gender, there was no difference between the groups [(12)].

Our studied groups were similar as regard the maternal age. This was in contrast to a study done by ***Abu-Zaid et al.***, which indicated that a significant contributing factor to the prevalence of PE in pregnancy is advanced maternal age, defined as greater than or equivalent to 35 years[(13)].

In our study, Apgar score was substantially less in PE with IUGR compared to PE without IUGR, also PE in comparison to controls had significantly lower Apgar. This agrees with the research by ***Sirenden et al.,*** that found that severe PE cases had considerably lower Apgar scores, birth weight [(14)]. This contrasts the study of ***AL-Bayati et al.***, which examined the impact of preeclampsia on the number of nucleated red blood cells in maternal and cord blood as a sign of fetal impairment. Preeclamptic and control groups' Apgar scores did not differ significantly from each other in the study population of 100 pregnant women, which was separated into equal preeclampsia and control groups [(15)].

White blood cell production is reported to be commonly affected by preeclampsia. Preeclampsia and the resulting uteroplacental insufficiency may prevent fetal bone marrow from producing cells of the myeloid lineage, which is evidenced by a decrease in neutrophil production. Reduced levels of granulocyte colony stimulating factor (G-CSF) and diminished neutrophil storage pools are also connected with the neutropenia caused by maternal preeclampsia [(16)]. This was similar to our results where the TLC was significantly lower in PE compared to control. Moreover, it was lower in PE with IUGR compared to PE without IUGR.

It is unclear what causes thrombocytopenia in newborns of preeclamptic moms. One possible mechanism is that preeclampsia and the resulting fetal hypoxia directly inhibit the growth of megakaryocytes. Studies demonstrating severe megakaryo-cytopoeitic abnormalities in growth-restricted newborns without evidence of enhanced platelet breakdown confirm this [(16)]. Similarly, our patients' platelets count was significantly lower in PE compared to control. Moreover, it was lower in PE with IUGR compared to PE without IUGR. That was in accordance with ***Thalor et al***. who not only compared the platelet count but the platelet indices which showed a significant difference between newborns of PE mothers and the controls and they also suggested that we can use the platelet indices as markers for the severity of PE[(17)].

The mean NRBC count in preeclampsia was assessed in the study by ***Darkhaneh et al.*** and it was decided that the NRBC were useful as independent predictive variables of perinatal problems. They contrasted the NRBC in the umbilical cords of term newborns delivered to 50 preeclamptic women with 150 healthy mothers. Contrary to our findings, the level of umbilical cord haemoglobin between the groups did not differ when the gestational age was matched [(18)].

In terms of pH, significant decrease was found in PE with IUGR compared to PE without IUGR, also both groups had typically lower pH values than control. Compared to a study done by ***Demir et al***. who did not find a difference between cord blood pH between mothers with PE compared to controls. [(19)]

In our study, cord blood NRBCs count were significantly higher in PE patients compared to controls [24 (15.25-40), 2(1-4) NRBCs/100 WBCs, respectively]. Moreover higher in PE with IUGR compared to PE without IUGR [39.5(27.25-60), 16(12-20.25) NRBCs/100 WBCs, respectively].

The best cutoff NRBC value to discriminate newborns of non PE mothers from newborns of PE mothers was ≥ 8 NRBCs/100 WBCs (sensitivity 94%; specificity 96%; PPV 97.9%; NPV 88.9%) while the best cutoff NRBCs value to discriminate newborns of PE mothers with IUGR from PE without IUGR was ≥ 22 NRBCs/100 WBCs (sensitivity 86%; specificity 84%; PPV 84.3%; NPV 85.7%).

This was in agreement with the research done comparing the preeclampsia and control groups, they evaluated the effects of preeclampsia on the cord blood and maternal NRBC count and compared the NRBC count and neonatal outcome. 100 women in all were studied, of which 50 had preeclampsia and 50 were healthy expectant mothers. According to their findings, PE women's cord blood had greater NRBC counts (40.0–85.1 NRBCs/100 WBCs) than controls (5.9–6.3 NRBCs/100 WBCs). Additionally, the cord blood NRBC count was considerably higher in preeclampsia cases involving IUGR newborns (83.0–133.4 NRBCs/100 WBCs) compared to AGA babies (17.9–26.8). As a result, the cNRBC count can be utilized to distinguish between newborns with growth restrictions and those that are fundamentally small [(20)].

In comparison to the control group (8.677.49 NRBCs/100 WBCs), PE women's cord blood had significantly higher nucleated red blood cell counts (12.448.25 NRBCs/100 WBCs), according to a study by ***AL-Bayati et al***. who attributed the rise in NRBC count to an increased erythrocyte synthesis as a protective strategy against a placenta that produced relatively little oxygen [(15)].

We found that NRBC was negatively correlated to gestational age and birth weight, in both PEgroups, while not correlated in control group. Similarly, ***Kil et al.*** who found that the average perinatal NRBC count in newborns with very low birth weights; is inversely related to birth weight and gestational age, showing a significant peak before delivery and a steady fall afterward. Additionally, they revealed a strong link between having an SGA and a rise in the number of NRBCs [(21)].

Birth weight below 2500 g and IUGR were substantially associated with a higher NRBC count in the PE group rather than the control group according to a study by *AL-Bayati et al.* This may be due to preeclampsia's ability to cause chronic hypoxia, which leads to the low birth weight, IUGR, and elevated NRBC count but not the control group's [(15)]. In contrast, ***Hebbar et al's*** study in 2014 indicated that neither the preeclampsia groups nor the control group, had any differences in the cord blood NRBCs count as a function of gestational age [(20)].

We observed no correlation between platelet counts and cord blood NRBCs count. A positive correlation was found between NRBCs count and hemoglobin level in IUGR. Contrarily, ***Perri et al.*** examined the relationship between increased NRBCs and pregnancy length by contrasting cord NRBCs with cord pH and other demographic and clinical factors. While no significant link was found between the NRBC count and the neonates' haemoglobin or hematocrit, univariate regression analysis (conducted on all 225 cases) showed a significant association between elevated NRBC counts and low thrombocytenia [(22)].

In our study, the NRBCs showed inverse correlation with pH and Apgar in PE with IUGR and PE without IUGR, while not correlated in control group. According to ***Boskabadi et al's*** study, which compared neonates with asphyxia to controls who were in good health, NRBC counts were found in both groups of newborns. High levels of NRBCs were linked to more severe acidosis, a lower Apgar score, and a worse short-term prognosis. They discovered a statistically significant negative association between NRBC count and neonatal pH. When compared to infants who survived, the NRBC count was elevated in infants who later died and significantly correlated with the Sarnat's grade of encephalopathy [(23)].

According to ***Hebbar et al.*** , a newborn's low first-minute Apgar score and high NRBC level are both related. IUGR, low Apgar scores, and fetal academia (as determined by an umbilical arterial pH of less than 7) have all been found to be connected to a significant increase in the number of nucleated red blood cell in the cord blood [(20)].

## CONCLUSION

PE was found to cause a considerably higher cNRBCs compared to controls. Additionally, higher in PE with IUGR than PE without IUGR. cNRBCs count therefore has predictive value for IUGR and may aid in differentiating between fundamentally tiny newborns and growth-restricted babies.

## LIMITATIONS OF THE STUDY

A drawback of our study might be the relatively limited number of patients in the three groups who had different neonates' gestational ages.

**Acknowledgment:** none
**Conflict of interest:** none found
**Financial support and sponsorship:** none provided.

## REFERENCES

1. **Rolnik D, O'Gorman N, Roberge S *et al.* (2017):** Early screening and prevention of preterm pre-eclampsia with aspirin: time for clinical implementation. Ultrasound Obstet Gynecol., 50(5):551-6.
2. **Ren Z, Gao Y, Gao Y *et al.* (2021):** Distinct placental molecular processes associated with early-onset and late-onset preeclampsia. Theranostics, 11(10):5028.
3. **Remaeus K, Johansson K, Askling J *et al.* (2017):** Juvenile onset arthritis and pregnancy outcome: a population-based cohort study. Annals of the Rheumatic Diseases, 76(11):1809-14.
4. **Rana S, Burke S, Karumanchi S (2020):** Imbalances in circulating angiogenic factors in the pathophysiology of preeclampsia and related disorders. American Journal of Obstetrics and Gynecology, 226(2S):S1019-S1034.

5. **Guerby P, Tasta O, Swiader A *et al.* (2021):** Role of oxidative stress in the dysfunction of the placental endothelial nitric oxide synthase in preeclampsia. Redox biology,40:101861.
6. **Abd El-Wahed M, El-Farghali O, ElAbd H *et al.* (2017):** Metabolic derangements in IUGR neonates detected at birth using UPLC-MS. Egyptian Journal of Medical Human Genetics, 18(3):281-7.
7. **Burton G, Jauniaux (2018):** Pathophysiology of placental-derived fetal growth restriction. American journal of obstetrics and gynecology, 218(2):S745-61.
8. **Mueller N, Zhang M, Hoyo C *et al.* (2019):** Does cesarean delivery impact infant weight gain and adiposity over the first year of life?. International Journal of Obesity,43(8):1549-55.
9. **Elsokkary M, Mamdouh A, Nossair W *et al.* (2019):** Significance of assay of nucleated RBCs in umbilical cord blood in neonates with meconium-stained amniotic fluid. The Journal of Maternal-Fetal & Neonatal Medicine, 32(3):483-7.
10. **Catarino C, Santos-Silva A, Belo L *et al.* (2012):** Inflammatory disturbances in preeclampsia: relationship between maternal and umbilical cord blood. Journal of pregnancy, 2012: 684384. doi: 10.1155/2012/684384
11. **Groom K, Poppe K, North R *et al.* (2007):** Small-for-gestational-age infants classified by customized or population birthweight centiles: impact of gestational age at delivery. Am J Obstet Gynecol., 197(3): 239.e1-5
12. **Tokmak A, Güney G, Aksoy R *et al.* (2014):** May maternal anti-mullerian hormone levels predict adverse maternal and perinatal outcomes in preeclampsia? J Matern Fetal Neonatal Med., 10:1-6.
13. **Abu-Zaid A, Alomari M, Al-Hayani M *et al.* (2020):** Advanced maternal age and the frequency of pre-eclampsia- a single-center crosssectional study from Saudi Arabia. J. Evolution Med. Dent. Sci., 9(37):2726- 2729, DOI: 10.14260/jemds/2020/592.
14. **Sirenden H, Suarno I, Arsyad M A *et al.* (2020):** Birth weight, Apgar score, and fetal complications in mothers with severe preeclampsia**.** Enfermeria Clinica, 30:533-536
15. **AL-Bayati M, Jameel B, Suhial T *et al.* (2011):** Maternal and Cord Blood Nucleated Red Blood Cells Count in Women with Preeclampsia. Iraqi J Comm Med., 24(4):302-307.
16. **Backes C, Markham K, Moorehead P *et al.* (2011):** Maternal Preeclampsia and Neonatal Outcomes. doi: 10.1155/2011/214365
17. **Thalor N, Singh K, Pujani M *et al.* (2019):** A correlatiom between platelet indices and preeclampsia. Hematol Transus Cell Ther.,41(2):129-133.
18. **Darkhaneh R, Ghanbari A, Asgharnia M *et al.* (2013):** Comparison of nucleated red blood cells in the umbilical cord of term neonates in healthy women and women with preeclampsia. Iran J Reprod Med., 11(1):25-30.
19. **Demir Ö, Sal H, Ozalp M *et al.* (2021):** Cord blood gas results of pregnancies complicated by preeclampsia and the relationship of these results with the amount of proteinuria**.** J. Obstet Gynaecol Res., 47(4):1322-1329.
20. **Hebbar S, Misha M, Rai L (2014):** Significance of Maternal and Cord Blood Nucleated Red Blood Cell Count in Pregnancies Complicated by Preeclampsia. Journal of pregnancy, 496416:1-7.
21. **Kil T, Han J, Kim J *et al.* (2011):** A study on the measurement of the nucleated red blood cell count based on birth weight and its correlation with perinatal prognosis in infants with very low birth weights. Korean J Pediatr., 54(2):69-78.
22. **Perri T, Ferber A, Digli A *et al.* (2014):** Nucleated Red Blood Cells in Uncomplicated Prolonged Pregnancy. American college of obstetricians and gynecologists, 104(2):372-376.
23. **Boskabadi H, Maamouri G, Sadeghian M *et al.* (2010):** Early Diagnosis of Perinatal Asphyxia by Nucleated Red Blood Cell Count: A Case-control Study. Archives of Iranian Medicine, 13(4):275-281.