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To investigate perinatal factors affecting platelet parameters in late preterm and term neonates.

Study Design
We retrospectively investigated platelet parameters including platelet counts (PLT), plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) on the first day of life in 134 late preterm and 357 term neonates admitted to our NICU from 2006 through 2017.

Results
PLT, MPV, PCT, PDW on the first day did not significantly differ between the two groups.

In term neonates, multivariate analysis revealed that PCT correlated with small for gestational age (SGA) (β =-0.135, P =0.002) and Apgar score at 5 min (β =0.114, P = 0.032). PLT was associated with SGA (β =-0.225, P =0.001), Apgar score at 5 min (β =0.025, P = 0.008) and pregnancy-induced hypertension PIH (β =-0.112, P =0.033).

In late preterm neonates, multivariate analysis revealed that PLT and PCT were associated with SGA, whereas no factors associated with PDW and MPV were found.

In all patients studied, chorioamniotitis (CAM) was significantly associated with MPV (CAM=10.4 fl vs. no CAM=9.6 fl, P <0.001). Multivariate analysis showed that SGA was associated with PCT and PDW. Furthermore, SGA (β =-0.252, P <0.001) and Apgar score at 5 min. (β =0.096, P =0.031) were associated with PLT.

Conclusion
This study demonstrates that different maternal and neonatal complications affect platelet parameters in late preterm and term neonates.

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Title
Perinatal factors affecting platelet parameters in late preterm and term neonates.

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Running title: Platelet parameters in late and term neonates

Keywords: platelet parameters, mean platelet volume, late preterm neonates
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Abstract

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Results

PLT, MPV, PCT, PDW on the first day did not significantly differ between the two groups.

In term neonates, multivariate analysis revealed that PCT correlated with small for gestational age (SGA) ($\beta=-0.135, P=0.002$) and Apgar score at 5 min ($\beta=0.114, P=0.032$). PLT was associated with SGA ($\beta=-0.225, P=0.001$), Apgar score at 5 min ($\beta=0.025, P=0.008$) and pregnancy-induced hypertension PIH ($\beta=-0.112, P=0.033$).
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In late preterm neonates, multivariate analysis revealed that PLT and PCT were associated with SGA, whereas no factors associated with PDW and MPV were found. In all patients studied, chorioamnionitis (CAM) was significantly associated with MPV (CAM=10.4 fl vs. no CAM=9.6 fl, $P<0.001$). Multivariate analysis showed that SGA was associated with PCT and PDW. Furthermore, SGA ($\beta=-0.252$, $P<0.001$) and Apgar score at 5 min. ($\beta=0.096$, $P=0.031$) were associated with PLT.

**Conclusion**

This study demonstrates that different maternal and neonatal complications affect platelet parameters in late preterm and term neonates.
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Introduction

Platelets parameters are associated with various physiological and pathological functions in various disease diseases (1,2,3). Platelet production is a complex process arising from the proliferation and differentiation of megakaryocytes under the stimulating influence of thrombopoietin. Platelet function in premature neonates is immature. Previous research indicated that low birth weight infants were at almost 2.5-fold increased risk for thrombocytopenia (4). On the other hand, elevated mean platelet volume (MPV), platelet distribution width (PDW), and increased plateletcrit (PCT) are associated with neonatal disease such as sepsis, fungal infection and intraventricular hemorrhage (5, 6, 7, 8). Among extremely low birth weight neonates born to mothers with preeclampsia, the MPV/platelet count (PLT) ratio at birth significantly correlated with mortality (9). Also, changes of PDW during the neonatal period were associated with thrombocytopenia with neonatal sepsis in very low birth weight infants (10). However, few studies have addressed whether perinatal factors may be associated with platelet parameters (PCT, PLT, MPV and PDW) at birth in a large cohort of late preterm and term neonates. The objective of this study was to investigate the factors affecting platelet parameters at birth in late preterm and term neonates.
The opening sentence of the Introduction is very vague and not compelling. Please be more specific and deliberate in your writing.

What is your hypothesis? It's not clear what you are adding to the existing body of knowledge.

What factors? What comparisons? What are the variables you are interested in studying. At this point, this sounds like an observational study, so please state that explicitly.

Why was analysis on preterm babies not performed? That data is discussed in the introduction, but you do not provide a rationale for why it is not included in this study. Why did you limit to term and late preterm?
Methods

Study design and population

This retrospective, single center, cohort study examined records from 2006 through 2017 at the neonatal intensive care unit (NICU) of Fukushima Medical University Hospital (FMU). The Ethics Committee of FMU, guided by local policy, national law, and the World Medical Association Declaration of Helsinki, approved this study without requiring informed consent from guardians. Of 1517 neonates admitted to our NICU between January 2006 and December 2017, there were 491 born at term or late preterm (weeks 35-36). Late preterm neonates and full term neonates numbered 134 and 357, respectively. Exclusion criteria were congenital anomalies, neonatal alloimmune thrombocytopenia, and neonates not tested within 12 hours of birth.

Platelet parameter measurements

Blood samples were collected through umbilical cord or peripheral venipuncture to measure PLT, PCT, MPV and PDW of each newborn. Complete blood counts were measured using a Sysmex CS-5100 coagulation analyzer (Sysmex, Kobe, Japan) on admission.
When were these samples collected? Beginning of Day of Life 1? At the end? Any time in the first 24 hours? This will confound your results significantly.

One of the factors you have failed to examine is how many babies required resuscitation at birth with epinephrine? Epinephrine has been reported to cause platelet aggregation as well as recruitment into the circulation. See Kjeldsen SE, Weder AB, Egan B, Neubig R, Zweifler AJ, Julius S. Effect of circulating epinephrine on platelet function and hematocrit. *Hypertension*. 1995;25(5):1096–1105.

Furthermore, reactivity to epinephrine via ADP and thromboxane differs between neonates and adults. Rajasekhar D, Barnard MR, Bednarek FJ, Michelson AD. Platelet hyporeactivity in very low birth weight neonates. *Thromb Haemost*. 1997;77(5):1002–1007.

Therefore it is important to note what the exposure to resuscitation and epinephrine is in these subjects.
Prenatal and postnatal risk factors

Platelet parameters were compared with demographic variables including gender, birth weight (BW), and gestational age (GA). Furthermore, we considered pregnancy-induced hypertension (PIH), chorioamnionitis (CAM), premature rupture of membranes (PROM), and placental abruption (PA) as possible prenatal risk factors, and small for gestational age (SGA, birth weight <10th percentile), appropriate for gestational age (AGA, birth weight >10th percentile), respiratory distress syndrome (RDS), and Apgar score as factors possibly associated with platelet parameters.

Statistical analysis

Platelet parameters from medical records were rendered as medians of non-normally distributed continuous variables. The Mann-Whitney U-test was performed to analyze nonparametric data. Likewise, correlations between BW, GA, and Apgar score versus
It would have been nice if platelet morphology was examined via microscopy on peripheral smears
platelet parameters were also investigated using Spearman’s rank correlation $(r)$. Moreover, the variables at $P < 0.05$ in univariate analysis were entered into a multiple regression analysis to identify independent prognostic factors.

SPSS for Mac, release 25.0 (SPSS, Chicago, IL) was used for statistical analyses with $P < 0.05$ considered to be statistically significant.

**Results**

Table 1 shows platelet parameters in late preterm and term neonates. There are no significant differences in platelet parameters between late preterm and term neonates. Figures 1A and 1B show significant correlation between BW and PLT, but none between GA and PLT. Likewise, Figures 1C and 1D show significant correlation between BW and PCT, but none between GA and PCT.

**Table 1. Platelet parameters in late preterm and term neonates**

|                  | Late preterm (n=134) | Term (n=357) | p-value |
|------------------|----------------------|--------------|---------|
| GA (weeks)       | 36.0                 | 38.2         | <0.001  |
| BW (grams)       | 2234                 | 2758         | <0.001  |
| PCT (%)          | 0.24                 | 0.25         | 0.492   |
| PDW              | 11.3                 | 11.3         | 0.701   |
| MPV (fl)         | 9.8                  | 9.8          | 0.879   |
Here it would be very important to separate the term and late preterm subjects by AGA and SGA status. So have four columns instead of two.
GA, gestational age; BW, birth weight; PCT, plateletcrit; PDW, platelet distribution width; MPV, mean platelet volume; PLT, platelet count.

Tables 2 and 3 outline the results of univariate and multivariate analyses for the correlation between perinatal factors and platelet parameters in preterm and term neonates, respectively.

As shown in Table 2, in term neonates, MPV and PDW were associated with CAM (CAM=10.4 fl vs. no CAM=9.6 fl, \( P = 0.001 \)) and PROM (PROM=10.3 % vs. no PROM=11.3 %, \( P = 0.049 \)), respectively. Multivariate analysis revealed that PCT correlated with SGA (\( \beta = -0.135, P = 0.002 \)) and Apgar score at 5 min (\( \beta = 0.114, P = 0.032 \)). PLT was associated with SGA (\( \beta = -0.225, P = 0.001 \)), Apgar score at 5 min (\( \beta = 0.025, P = 0.008 \)) and PIH (\( \beta = -0.112, P = 0.033 \)).

As shown in Table 3, univariate analysis revealed that PDW was correlated with PIH in late preterm neonates (PIH=10.4 fl vs. no PIH=11.3 fl, \( P = 0.038 \)). Multivariate analysis revealed that PLT and PCT were associated with SGA, whereas no factors associated with PDW and MPV were found in late preterm neonates.

**Table 2. Factors affecting platelet parameters in term neonates.**

| PLT (×10^3/μL) | 25.6 | 25.6 | 0.973 |
|----------------|------|------|-------|


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|                  | PCT (%) | PDW (%) | MPV (fl) | PLT (×10³/μL) |
|------------------|---------|---------|----------|----------------|
|                  | univariate analysis | multivariate analysis | univariate analysis | univariate analysis | multivariate analysis |
| Male (n=182)     |         |         |          |                |
| Yes              | 0.24    | 11.2    | 9.7      | 25.0           |
| No               | 0.25    | 11.4    | 9.9      | 26.0           |
| p-value          | 0.218   | 0.49    | 0.694    | 0.113          |
| RDS (n=26)       |         |         |          |                |
| Yes              | 0.23    | 11.1    | 9.8      | 22.3           |
| No               | 0.25    | 11.3    | 9.8      | 25.6           |
| p-value          | 0.305   | 0.789   | 0.545    | 0.487          |
| SGA (n=50)       |         |         |          |                |
| Yes              | 0.21    | 11.9    | 10       | 20.7           |
| No               | 0.25    | 11.2    | 9.7      | 25.9           |
| p-value          | 0.000   | 0.055   | 0.161    | 0.000          |
| Death (n=19)     |         |         |          |                |
| Yes              | 0.24    | 11.8    | 10.3     | 23.2           |
| No               | 0.25    | 11.2    | 9.7      | 25.5           |
| p-value          | 0.381   | 0.062   | 0.063    | 0.099          |
| PROM (n=10)      |         |         |          |                |
| Yes              | 0.22    | 10.3    | 9.6      | 23.9           |
| No               | 0.25    | 11.3    | 9.8      | 25.6           |
| p-value          | 0.226   | 0.049   | 0.436    | 0.254          |
| CAM (n=9)        |         |         |          |                |
| Yes              | 0.21    | 11.4    | 10.4     | 21.4           |
| No               | 0.25    | 11.4    | 9.6      | 26.1           |
| p-value          | 0.584   | 0.125   | 0.001    | 0.121          |
| PA (n=5)         |         |         |          |                |
| Yes              | 0.21    | 11.1    | 10.2     | 23.1           |
| No               | 0.25    | 11.3    | 9.7      | 25.5           |
| p-value          | 0.13    | 0.897   | 0.829    | 0.469          |

Note: Values in parentheses indicate p-values.
What is your definition of SGA?
Table 3. Factors affecting platelet parameters in late preterm neonates.

| Factor       | Yes (n=7) | No (n=7) | p-value (β) | r      | p-value (β) | r      | p-value (β) | r      | p-value (β) | r      |
|--------------|-----------|----------|-------------|--------|-------------|--------|-------------|--------|-------------|--------|
| PIH          |           |          |             |        |             |        |             |        |             |        |
| Yes          | 0.19      | 10.9     | 9.7         | 20.1   |              |        |             |        |             |        |
| No           | 0.50      | 11.3     | 9.8         | 25.6   |              |        |             |        |             |        |
| p-value (β)  | 0.003     | 0.050    | -0.104      | 0.242  | 0.618        | 0.025  | 0.033       | -0.112 | 0.006       | 0.008  |
| GA (week)    |           |          |             |        |             |        |             |        |             |        |
| r            | -0.039    | -0.044   | 0.077       | -0.063 |              |        |             |        |             |        |
| p-value      | 0.469     | 0.419    | 0.149       | 0.236  |              |        |             |        |             |        |
| BW (gram)    |           |          |             |        |             |        |             |        |             |        |
| r            | 0.130     | -0.099   | 0.003       | 0.108  |              |        |             |        |             |        |
| p-value (β)  | 0.014     | 0.726    | 0.023       | 0.063  | 0.952        | 0.041  | 0.821       | -0.015 | 0.167       | -0.139 |
| AP1          |           |          |             |        |             |        |             |        |             |        |
| r            | 0.096     | -0.087   | -0.054      | 0.113  |              |        |             |        |             |        |
| p-value      | 0.074     | 0.347    | 0.320       | 0.036  | 0.167        | 0.006  | 0.008       | 0.265  | 0.153       |        |
| AP5          |           |          |             |        |             |        |             |        |             |        |
| p-value (β)  | 0.014     | 0.032    | 0.114       | 0.148  | 0.144        | 0.006  | 0.008       | 0.265  | 0.153       |        |

PCT, platelet count; PDW, platelet distribution width; MPV, mean platelet volume; PLT, platelet count; GA, gestational age; BW, birth weight; RDS, respiratory distress syndrome; SGA, small for gestational age; AP1, Apgar score at 1 min.; AP5, Apgar score at 5 min.; PROM, premature rupture of membranes; CAM, chorioamnionitis; PA, placental abruption; PIH, pregnancy-induced hypertension. Significant correlation between GA, BW, Apgar score and platelet parameters were analyzed using Spearman’s rank correlation (r). β means standardized regression coefficient.
You have omitted definitions for several of these variables. Is CAM clinical or culture proven? What is the definition of clinical chorio at your institution?
| Condition  | Male (n=75) | RDS (n=14) | SGA (n=50) | Death (n=6) | PROM (n=16) | CAM (n=9) | PA (n=10) |
|------------|-------------|------------|------------|-------------|-------------|-----------|-----------|
|            | PCT (%)     | PDW (%)    | MPV (fl)   | PLT (×10^3/μL) | PCT (%)     | PDW (%)    | MPV (fl)   | PLT (×10^3/μL) | PCT (%)     | PDW (%)    | MPV (fl)   | PLT (×10^3/μL) | PCT (%)     | PDW (%)    | MPV (fl)   | PLT (×10^3/μL) |
|            | univariate analysis | multivariate analysis | univariate analysis | univariate analysis | univariate analysis | multivariate analysis | univariate analysis | multivariate analysis | univariate analysis | multivariate analysis | univariate analysis | multivariate analysis | univariate analysis | multivariate analysis | univariate analysis | multivariate analysis |
| Yes        | 0.24        | 11.2       | 9.8        | 24.9        | 0.24        | 11.2       | 9.7        | 23.6        | 0.24        | 11.7       | 10         | 22.1        | 0.25        | 11.2       | 9.8        | 27.1        |
| No         | 0.24        | 11.2       | 9.9        | 25.8        | 0.22        | 11.0       | 9.9        | 25.8        | 0.24        | 11.2       | 9.8        | 27.1        | 0.25        | 11.2       | 9.8        | 27.1        |
| p-value    | 0.569       | 0.971      | 0.217      | 0.905       | 0.101       | 0.434      | 0.366      | 0.243       | 0.640       | 0.173      | 0.897      | 0.407       | 0.226       | 0.500      | 0.028 (0.065) | 0.511       |
|            | p-value (β) | 0.002      | 0.024 (-0.265) | 0.119       | 0.296       | 0.001      | 0.019 (-0.275) | 0.226       | 0.500      | 0.028 (0.065) | 0.511       | 0.24        | 11.0       | 9.9        | 24.9        |
|            |            |            |            |              |            |            |            |              |            |            |            |              |            |            |            |              |

**Notes:**
- PCT: Procalcitonin (pg/mL), PDW: Platelet Distribution Width (%), MPV: Mean Platelet Volume (fl), PLT: Platelet Count (×10^3/μL).
- Univariate and multivariate analyses are performed.
- p-values are indicated for each condition.
- β-values are provided for p-values of 0.05 or below.
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PCT, platelet count; PDW, platelet distribution width; MPV, mean platelet volume; PLT, platelet count; GA, gestational age; BW, birth weight; RDS, respiratory distress syndrome; SGA, small for gestational age; AP1, Apgar score at 1 min.; AP5, Apgar score at 5 min.; PROM, premature rupture of membranes; CAM, chorioamnionitis; PA, placental abruption; PIH, pregnancy-induced hypertension. Significant correlation between GA, BW, Apgar score and platelet parameters were analyzed using Spearman’s rank correlation (r). β means standardized regression coefficient.

When all patients were studied, CAM was significantly associated with MPV ((CAM=10.4 fl vs. no CAM=9.6 fl, P<0.001).

Multivariate analysis showed that SGA was associated with PCT and PDW. Furthermore, SGA (β=-0.252, P<0.001) and Apgar score at 5 min. (β=0.096, P=0.031) were associated with PLT (Table 4).
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Next, we compared the differences of platelet parameters between SGA and AGA (Table 5). Table 5 showed that PLT, and PCT were significantly decreased and PDW was significantly increased in SGA neonates compared with AGA neonates.

Table 4. Factors affecting platelet parameters in late preterm and term neonates.

|        | PCT (%) univariate analysis | PCT (%) multivariate analysis | PDW (%) univariate analysis | PDW (%) multivariate analysis | MPV (fl) univariate analysis | PLT (×10^3/μL) univariate analysis | PLT (×10^3/μL) multivariate analysis |
|--------|-----------------------------|-------------------------------|-----------------------------|-------------------------------|-------------------------------|------------------------------------|-------------------------------------|
| Male (n=259) |                              |                               |                             |                               |                              |                                    |                                     |
| Yes    | 0.24                        | 11.2                          | 9.7                         | 25.4                          |                               |                                    |                                     |
| No     | 0.25                        | 11.4                          | 9.9                         | 26.6                          |                               |                                    |                                     |
| p-value | 0.193                       | 0.561                         | 0.293                       | 0.213                         |                               |                                    |                                     |
| RDS (n=40) |                              |                               |                             |                               |                              |                                    |                                     |
| Yes    | 0.25                        | 11.1                          | 9.7                         | 23.3                          |                               |                                    |                                     |
| No     | 0.22                        | 11.3                          | 9.8                         | 25.6                          |                               |                                    |                                     |
| p-value | 0.073                       | 0.525                         | 0.975                       | 0.229                         |                               |                                    |                                     |
| SGA (n=87) |                              |                               |                             |                               |                              |                                    |                                     |
| Yes    | 0.21                        | 11.6                          | 9.9                         | 22.1                          |                               |                                    |                                     |
| No     | 0.25                        | 11.2                          | 9.8                         | 25.9                          |                               |                                    |                                     |
| p-value | 0.001                       | 0.004 (-0.265)                | 0.016                       | 0.003 (0.137)                | 0.077                        | 0.001                               | 0.001 (-0.252)                      |
| Death (n=25) |                              |                               |                             |                               |                              |                                    |                                     |
| Yes    | 0.24                        | 11.8                          | 10.3                        | 26.5                          |                               |                                    |                                     |
| No     | 0.24                        | 11.2                          | 9.8                         | 25.6                          |                               |                                    |                                     |
| p-value | 0.381                       | 0.062                         | 0.114                       | 0.099                         |                               |                                    |                                     |
| PROM (n=26) |                              |                               |                             |                               |                              |                                    |                                     |
| Yes    | 0.24                        | 10.9                          | 9.8                         | 23.9                          |                               |                                    |                                     |
| No     | 0.24                        | 11.3                          | 9.9                         | 25.6                          |                               |                                    |                                     |
| p-value | 0.826                       | 0.513                         | 0.225                       | 0.826                         |                               |                                    |                                     |
| CAM (n=19) |                              |                               |                             |                               |                              |                                    |                                     |
| Yes    | 0.21                        | 11.4                          | 10.4                        | 21.4                          |                               |                                    |                                     |
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|              | GA (week) | BW (gram) | AP1 | AP5 |
|--------------|-----------|-----------|-----|-----|
| No           | 0.25      | 11.4      | 9.6 | 26.1|
| p-value      | 0.842     | 0.056     | <0.001 | 0.163|
| PA (n=15)    | Yes       | 0.21      | 11.1 | 10.2 | 23.1|
|              | No        | 0.25      | 11.3 | 9.7  | 25.5|
| p-value      | 0.497     | 0.558     | 0.372 | 0.058|
| PIH (n=15)   | Yes       | 0.20      | 10.9 | 9.7  | 20.1|
|              | No        | 0.24      | 11.3 | 9.8  | 25.6|
| p-value(β)   | 0.012     | 0.089(-0.076) | 0.019 | 0.138 (-0.068) | 0.071 | 0.058|
| GA (week)    | r         | -0.039    | -0.044 | 0.077 | -0.063|
| p-value      | 0.891     | 0.862     | 0.562 | 0.319|
| BW (gram)    | r         | 0.130     | -0.099 | 0.003 | 0.108|
| p-value(β)   | 0.002     | 0.766(0.017) | 0.280 | 0.655 | 0.015 | 0.781 (-0.015)|
| AP1          | r         | 0.096     | -0.087 | -0.054 | 0.113|
| p-value      | 0.135     | 0.334     | 0.475 | 0.052|
| AP5          | r         | 0.132     | -0.150 | -0.079 | 0.153|
| p-value(β)   | 0.069     | 0.041     | 0.316 (-0.046) | 0.421 | 0.020 | 0.031 (0.096)|

PCT, plateletcrit; PDW, platelet distribution width; MPV, mean platelet volume; PLT, platelet count; GA, gestational age; BW, birth weight; RDS, respiratory distress syndrome; SGA, small for gestational age; AP1, Apgar score at 1 min; AP5, Apgar score at 5 min; PROM, premature rupture of membranes; CAM, chorioamnionitis; PA, placental abruption; PIH, pregnancy-induced hypertension. Significant correlation between GA, BW, Apgar score and platelet parameters were analyzed using Spearman’s rank correlation (r). β means standardized regression coefficient.
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Table 5. Platelet parameters in SGA and AGA neonates.

|                  | SGA (n=87) | AGA (n=404) | p-value |
|------------------|------------|-------------|---------|
| GA (weeks)       | 37.1       | 38.1        | <0.001  |
| BW (gram)        | 1808       | 2752        | <0.001  |
| PCT (%)          | 0.21       | 0.25        | <0.001  |
| PDW              | 11.8       | 11.2        | 0.016   |
| MPV (fl)         | 10.0       | 9.7         | 0.077   |
| PLT ($\times 10^3/\mu$L) | 21.2 | 26.1 | <0.001 |

MPV, mean platelet volume; PDW, platelet distribution width; MPV, mean platelet volume; PLT, platelet; PCT, plateletcrit.

Discussion

This large cohort showed no differences in platelet parameters at birth between late preterm and term neonates. Previous reports indicated that PLT and PCT were lower in late preterm neonates compared with term neonates (11,12). Furthermore, they suggested that GA was significantly correlated with PLT; however, in our study, GA did not correlate with PLT (11). Instead, there was positive correlation between BW and PLT in preterm and term neonates by univariate analysis. These differences may be due to differences in sample size and time of sampling. Other research included 129 neonates: 58 late preterm and 71 full term. Moreover, they found that
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PLT measured using cord blood was associated with GA and BW in late preterm and term neonates. In our study, we used cord blood and venous blood at admission to NICU. The mean time of sampling in this study was just under 2 hours after birth (data not shown).

This study also demonstrates that various maternal and neonatal factors affect platelet parameters in late preterm and term neonates. Especially, late preterm and term SGA neonates had lower PLT and PCT compared with AGA neonates as previously described (13,14). Lower PLT in SGA indicates the immaturity of thrombopoiesis. (15,16). Roberts suggested that reduced platelet production was characteristic of preterm neonates and they had fewer circulating megakaryocytes (17). Another study reported that plasma thrombopoietin concentrations were low in thrombocytopenic newborns, indicative of inadequate up-regulation of TPO production (18). Platelets are produced in the fetal liver, with production transferred to bone marrow in the third trimester (19). The liver is one of the first organs to be exposed to growth restriction.

On the other hand, Apgar score at 5 minutes was associated with lower PLT in late preterm and term neonates. Some studies previously showed that low Apgar score at 5 minutes was related to thrombocytopenia (20,21). Mario et al showed that SGA, low Apgar score at 5 minutes, cesarean delivery and lower gestational age were risk factors for thrombocytopenia in preterm deliveries between 27 and 35 weeks of gestation (20). To date, perinatal asphyxia has been associated with thrombocytopenia in late preterm and
This needs to be clearly stated in the methods.

You also need to differentiate which values were collected from cord and which were from venous samples. Were these values compared to one another? If not, it would be vital to know if there is a difference in parameters from these two methods of sampling.
term neonates (4). In murine models, it is known that hypoxia affects megakaryocyte progenitors and induces thrombocytopenia (22,23). Castle et al reported that severe hypoxia significantly shortened the survival of platelets in a murine model (24). Boutaybi et al found that low Apgar score at 10 min and high serum lactate were risk factors of early-onset thrombocytopenia (25). However, there are few reports about the relationship between perinatal factors and platelet parameters among large cohorts of premature newborns.

The present study suggested that CAM was associated with MPV in term neonates. However, PROM was not associated with MPV as in a previous study (26). Recently, a retrospective study has reported significant correlation between MPV and intrauterine infection in neonates with thrombocytopenia and leukopenia at birth (18,27). Since CAM was indicative of intrauterine infection, our results are consonant with previous studies. Furthermore, PDW in SGA neonates was significantly higher than those of AGA neonates. This result agrees with a previous study (28). Recently, elevated PDW was associated with poor prognosis of various conditions such as carcinoma and cardiovascular disease (1,29,30). Furthermore, Patrick et al reported that high MPV and PDW showed high specificity in neonates with late sepsis (31).
Determining exposure to epinephrine and resuscitation may help understand this better. See comment above.
Our study has several limitations. First, we used samples of cord blood and venous blood on admission. The timing of samples might affect platelet parameters. Second, we could not investigate the relationship between platelet parameters and sepsis because few of our preterm infants had sepsis at birth and we did not investigate changes of platelet parameters during the postnatal period. Some studies associated sepsis with elevated MPV in neonates during the postnatal period (31,32).

In summary, this study demonstrates that various maternal and neonatal factors affect platelet parameters in late preterm and term neonates. In particular, SGA and low Apgar score at 5 minutes were associated with lower PLT in late preterm and term neonates. CAM was significantly associated with MPV. Thus, this study demonstrates that different maternal and neonatal complications affect platelet parameters in late preterm and term neonates.

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Figure legends

Figure 1. Correlation between platelet count, plateletcrit, GA, and BW.

R means Spearman’s correlation coefficient.
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Figure 1

A

R = 0.04, p = 0.015

B

R = 0.004, p = 0.359

C

R = 0.04, p = 0.002

D

R = 0.002, p = 0.977
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