Are Leukocyte and Platelet Indices Associated with Small for Gestational Age Birth and/or Oligohydramnios?

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Abstract

Introduction: To investigate whether certain leukocyte and platelet indices predict Small for Gestational Age (SGA) birth and/or oligohydramnios.

Materials and Methods: In this retrospective study, 408 pregnant women were included, who didn’t have foreknown systemic diseases and other risk factors like drug use, smoking. Patients diagnosed with SGA birth (Group-I, n=59), SGA birth and oligohydramnios (Group-II, n=46), solely oligohydramnios (Group-III, n=23) and control group (Group-IV, n=280, matched for maternal age and body mass index) were selected from medical records. Leukocyte and platelet indices in first trimester and third trimester, demographic and obstetric data were obtained from medical records. Then, groups were compared.

Results: Maternal ages and body mass indices were similar among groups. Total leukocyte, neutrophil, lymphocyte and platelet counts, platelet indices (p<0.001), neutrophil to lymphocyte ratios (p<0.001) were significantly different between first and third trimester values in all patients. Platelet distribution width values of group-II in both trimester were significantly higher than ones of group-IV.

Conclusion: Most hematologic parameters were not associated with SGA birth and/or oligohydramnios, but it was clarified that they differ significantly between first and third trimester. A new prospective study with larger sample size may present more definitive results.

Keywords: Small for gestational age, oligohydramnios, platelet indices, platelet distribution width, leukocyte indices.

Introduction

Intrauterine growth restriction (IUGR) is widely accepted to be important for perinatal outcomes, and prediction of that is essential in the same way. In 1967, Battaglia and Lubchenco defined the babies whose weights lower than 10th percentile by means of gestational age as small for gestational age (SGA). The incidence of SGA was found to be 10%. These babies were showed to be at high risk for neonatal mortality. The more baby get smaller than 10th percentile, the more neonatal morbidity and mortality increase (1). Malnutrition, infections, genetic diseases, congenital malformations, placental and vascular diseases are main causes of IUGR, but they can also give way to SGA, too (2). The diagnosis of IUGR is a challenging clinical entity, because its diagnosis is largely based on dynamic pathologic processes, for example measurement of pathologic blood stream, namely Doppler evaluation. The diagnosis of SGA is based on customized growth charts. So, making the diagnosis of SGA is easier than of IUGR. Growth charts seem to be enough to make the diagnosis of SGA, irrespective of its etiology (3).

Oligohydramnios is a multifactorial clinical entity defined as diminished volume of amniotic fluid and an important diagnosis as well as growth disturbances mentioned above. Fetal development of musculoskeletal and bronchopulmonary systems are extremely vital to maintain a healthy life; the role of amniotic fluid is undeniable to make these come true. Furthermore, volume of amniotic fluid is also a determinant for growth restriction, because it supplies not only bronchopulmonary and musculoskeletal development, but also a space to allow fetus to grow outwards. Likewise, oligohydramnios and IUGR may share same destiny of pathogenesis; the placental insufficiency (4).

There have been several researches about pathogenesis of small for gestational age and oligohydramnios, but until now, haematologic parameters have not been studied except neutrophil activation (5), according to our comprehensive literature search. We aimed to determine associations among SGA and/or oligohydramnios and haematologic parameters.

Materials and Methods

A total of 128 patients diagnosed with SGA and/or oligohydramnios and 280 patients as a control group...
given as a unit of kg/m².

Body mass indices were calculated by using weight (kilogram, kg) and height (meters, m) of the patients, counts were irrespective from any infectious process.

Results in order to suggest that the high leukocyte levels as well as negative cervical and urinary culture all had to have normal C-reactive protein (CRP) obtained from medical records. The patients were

cocaine) and who have been smoking.

Haematologic parameters in first and third trimester, demographic data like maternal age, previous reproductive history, body weight and height, gestational age at birth, route for delivery, birthweight (BW), and gender of the neonate were obtained from medical records. The patients were all had to have normal C-reactive protein (CRP) levels as well as negative cervical and urinary culture results in order to suggest that the high leukocyte counts were irrespective from any infectious process.

Body mass indices were calculated by using weight (kilogram, kg) and height (meters, m) of the patients, given as a unit of kg/m².

All hematologic parameters were analyzed with LH780 hematological analyzer (Beckman Coulter, Fullerton, CA, USA), within two hours of blood sampling. Neutrophil to lymphocyte ratio (NLR) was calculated by proportioning absolute neutrophil count to absolute lymphocyte count. Likewise, Platelet to lymphocyte ratio (PLR) was calculated by proportioning absolute platelet count to absolute lymphocyte count.

After laboratory analyses had been recorded, groups were compared with eachother about demographic data and haematologic parameters, using the Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) software, version 17.0 for Windows. Distribution of the data was analyzed with Kolmogorov-Smirnov and Shapiro Wilk test. The data were presented as mean with standard deviation or median with minimum and maximum values of ranges for continuous variables, and as number with percentage for categorical variables. In comparisons between groups, Independent samples T test was used for parametric variables and Mann-Whitney U test was used for nonparametric variables. Proportions were compared with the Chi-square test. p<0.05 value was accepted as significant.

Results

Maternal ages and body mass indices were similar among groups because of matching groups. There were significant differences between anyone of study groups and Group-IV about reproductive history, except the abortus status between Group-III and Group-IV(Table 1). Gestational ages at birth in group-I (37.02 ± 2.56 years) and group-II (37.0 ± 2.74 years) were significantly lower than ones in the control group (38.68 ± 1.31 years) (p<0.001 and p<0.001, respectively) (Table 1). Birthweights (BWs) varied between 690 and 4500 grams (g) (3039.35±658.78 g). BWs in Group-I (2220.71±497.2 g), Group-II (2175.87±543.66 g) and Group-III (2862.17±577.67 g) were significantly lower than ones in the control group (3359.48±377.93 g). Delivery with cesarean section was more frequent in Group-I (69.5%) than other groups (Chi-square: 7.583, p=0.006). Gender of the baby did not differ among groups significantly (Chi-square: 3.86, p=0.277) as seen in Table 1.

Total leukocyte (white blood cell; WBC) counts (p<0.001), neutrophil counts (p<0.001), lymphocyte counts (p=0.002), platelet (PLT) counts (p<0.001), mean platelet volumes (MPV) (p<0.001), ‘platelet-crit’ values (PCT) (p<0.001), ‘platelet distribution width’ values (PDW) (p<0.001), ‘Platelet-large
cell ratio’ values (P-LCR) (p<0.001), neutrophil to lymphocyte ratios (NLR) (p<0.001) were significantly different between first and third trimester in all patients as seen in Table 2. Platelet to lymphocyte ratios (PLR) weren’t significantly different between first and third trimester in all population.

All these haematologic parameters were compared among four groups (Table III). About platelet counts in third trimester; those in Group-I (251.47±68.48 x10^9/L) were significantly higher than ones in the control group (228.71±61.49 x10^9/L). Platelet counts in Group-II and Group-III were higher than the values in Group-IV, but not significantly. In terms of PCT values in the third trimester, those in Group-I significantly higher than ones in the control group.

Comparison between Group-II and Group-IV revealed that both PDW in the first trimester and PDW in the third trimester values in group-II were significantly higher than ones in group-IV.

Furthermore, comparison between Group-I and Group-IV revealed that WBC in the third trimester to

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**Table 1.** Comparison of some demographic and haematologic parameters among four groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I (n=59)</th>
<th>Group II (n=46)</th>
<th>Group III (n=23)</th>
<th>Group IV (n=280)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.88±5.60</td>
<td>25.93±5.24</td>
<td>26.43±4.24</td>
<td>27.12±4.47</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.52±3.14</td>
<td>28.01±3.81</td>
<td>29.57±4.16</td>
<td>28.70±3.46</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Gravidity</td>
<td>2 (1-6)</td>
<td>1.5 (1-4)</td>
<td>1.5 (1-4)</td>
<td>2 (1-7)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Parity</td>
<td>0 (0-4)</td>
<td>0 (0-3)</td>
<td>0 (0-3)</td>
<td>1 (0-6)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Living Child</td>
<td>0 (0-4)</td>
<td>0 (0-3)</td>
<td>0 (0-3)</td>
<td>1 (0-6)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Abortus</td>
<td>0 (0-3)</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>0 (0-3)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Dilatation and Curettage</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
<td>0 (0-5)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Birthweight (grams)</td>
<td>2220.71±497.2</td>
<td>2175.87±543.66</td>
<td>2862.17±577.67</td>
<td>3359.48±377.93</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Gestational age at birth (weeks)</td>
<td>37.0±2.56</td>
<td>37.0±2.74</td>
<td>37.77±2.80</td>
<td>38.68±1.31</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Cesarean delivery rate (%)</td>
<td>69.5</td>
<td>565</td>
<td>565</td>
<td>48.6</td>
<td>0.003a</td>
</tr>
<tr>
<td>Gender of the Baby (%) (Male/Female)</td>
<td>42.4 / 57.6</td>
<td>43.5 / 56.5</td>
<td>65.2 / 34.8</td>
<td>48.2 / 51.8</td>
<td>0.414a</td>
</tr>
</tbody>
</table>

Group I: Polyhydramnios, Group II: SGA and Oligohydramnios, Group III: Oligohydramnios, Group IV: Control group.

a p value of the comparison between Group-I and Group-IV.
b p value of the comparison between Group-II and Group-IV.
c p value of the comparison between Group-III and Group-IV.

Cesarean delivery rates were given as number of percentage, reproductive history characteristics were given as median (minimum-maximum), and other values were given as mean ± standard deviation.
WBC in the first trimester ratio (WBC3/WBC1) values in group-I were significantly higher than in group-IV. Both NLR in the first trimester and NLR in the third trimester values were similar between two groups. However, abovementioned variables were not different between Group-III and Group-IV (Table 3).

**Discussion**

Most leukocyte indices and most platelet indices, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratios (PLR) in first or third trimester were not associated with SGA birth and/or oligohydramnios in our study, but it was clarified that they differ significantly between first and third trimester.

Similarity of groups in terms of maternal age and BMI has provided homogeneity and increased the probability of accurate evaluation. Birth weights in the study groups were significantly lower than in the control group, we attributed it to their complicated pregnancies. Gestational ages at birth were significantly lower in patients with SGA and it demonstrated that earlier intervention were warranted for these subjects.

Cesarean rate in the Oligohydramnios group was not significantly different from the control group, it’s disharmonious with previous studies by Varma et al (9), and Locatelli et al (4). Similarly, cesarean rate in the SGA and Oligohydramnios group was not significantly different from the control group. We found no explanation for this in the literature.

Diversity of haematologic parameters between first and third trimester makes us think that pregnancy is a changing process in itself, continuously. In a study it was found that the upper limit of leukocyte count increases from first to third trimester (10), this is consistent with our findings. Investigations about altered plasm volume and cellular content has revealed that the increase in the WBC count was largely due to increases in circulating segmented neutrophils and granulocytes whose absolute number was nearly doubled at term. It was said that the reason for the increased leukocytosis was still unclear, but it might have been caused by the elevated estrogen and cortisol levels (11).

In a previous study, Harita et al. found that patients who had SGA baby had had higher neutrophil counts in third trimester than patients in the control group, but there had been no difference between first trimester values (12). Confirming this idea, in a study by Johnston et al, it was showed that there was neutrophil activation in SGA pregnancies during the third trimester (5). In our study, no difference was found among neutrophil counts of groups in the first or in the third trimester. WBC3/WBC1 ratios were significantly higher in the Polyhydramnios group than the control group, consistent with the study by Harita et al (12). No significant difference was found between the SGA and Oligohydramnios group and the control group or between the Oligohydramnios...
group and the control group in terms of WBC3/WBC1 ratio. This variable should be widely investigated with further studies.

Platelet (PLT) counts of all patients in the first trimester were significantly higher than in the third trimester. It’s consistent with the literature, for example Pitkin and Witte (13), and O’Brien (14) showed that platelet counts were decreasing with advancing gestational age. In our study, MPV and PDW values of all patients in the third trimester were significantly higher than in the first trimester. Diminution of platelet counts and simultaneously enhancement of their volume and distribution width over the third trimester might be caused by destruction of them, regarding microangiopathic reasons, even in normal pregnancy. It has been well established in a study by Fay et al (15).

Platelet counts of the study groups in the third trimester were higher than the control group. Especially in the Polyhydramnios group, this

Table 3. Comparisons of some haematologic parameters among groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I (n=59)</th>
<th>Group II (n=46)</th>
<th>Group III (n=23)</th>
<th>Group IV (n=280)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLT1 (x10^9/L)</td>
<td>247.64 ±60.03</td>
<td>248.27 ±59.42</td>
<td>236.33 ±45.54</td>
<td>249.78 ±56.64</td>
<td>0.850^a</td>
</tr>
<tr>
<td>PLT3 (x10^9/L)</td>
<td>251.47 ±68.48</td>
<td>240.28 ±65.26</td>
<td>240.70 ±52.51</td>
<td>228.71 ±61.49</td>
<td>0.012^b</td>
</tr>
<tr>
<td>PCT1</td>
<td>0.25 ±0.06</td>
<td>0.26 ±0.05</td>
<td>0.25 ±0.04</td>
<td>0.26 ±0.05</td>
<td>0.514^c</td>
</tr>
<tr>
<td>PCT3</td>
<td>0.26 ±0.07</td>
<td>0.25 ±0.07</td>
<td>0.24 ±0.05</td>
<td>0.24 ±0.06</td>
<td>0.018^d</td>
</tr>
<tr>
<td>PDW1 (%)</td>
<td>13.57 ±2.11</td>
<td>13.79 ±2.05</td>
<td>12.80 ±2.43</td>
<td>12.80 ±2.05</td>
<td>0.058^e</td>
</tr>
<tr>
<td>PDW3 (%)</td>
<td>13.94 ±2.31</td>
<td>14.80 ±2.06</td>
<td>14.37 ±2.27</td>
<td>13.60 ±2.55</td>
<td>0.012^f</td>
</tr>
<tr>
<td>WBC3/WBC1</td>
<td>1.31 ±0.31</td>
<td>1.13 ±0.29</td>
<td>1.12 ±0.12</td>
<td>1.15 ±0.29</td>
<td>0.014^g</td>
</tr>
<tr>
<td>NLR1</td>
<td>2.90 ±0.96</td>
<td>3.35 ±1.39</td>
<td>2.70 ±0.76</td>
<td>3.32 ±1.36</td>
<td>0.223^h</td>
</tr>
<tr>
<td>NLR3</td>
<td>4.27 ±1.31</td>
<td>4.21 ±1.78</td>
<td>4.49 ±1.83</td>
<td>4.12 ±1.98</td>
<td>0.054^i</td>
</tr>
<tr>
<td>PLR1</td>
<td>126.73 ±44.77</td>
<td>122.49 ±40.03</td>
<td>108.89 ±19.49</td>
<td>131.14 ±41.54</td>
<td>0.532^j</td>
</tr>
<tr>
<td>PLR3</td>
<td>134.68 ±51.80</td>
<td>129.17 ±58.28</td>
<td>135.0 ±34.52</td>
<td>126.22 ±48.55</td>
<td>0.279^k</td>
</tr>
</tbody>
</table>

Group I: Polyhydramnios, Group II: SGA and Oligohydramnios, Group III: Oligohydramnios, Group IV: Control group.

^p value of the comparison between Group-I and Group-IV.

^p value of the comparison between Group-II and Group-IV.

^p value of the comparison between Group-III and Group-IV.

All values were given as mean ± standard deviation. PLT: Platelet count, PCT: Platelet-crit, PDW: Platelet distribution width, WBC: White blood cell count, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio. Numbers near the variables refer to them in which trimester of pregnancy.
difference reached statistical significance. Findings lead us to think that platelet counts decrease with advancing gestational age, increase with SGA and/or oligohydramnios.

PCT values of the Polyhydramnios group in the third trimester were significantly higher than ones of the control group, it seems to reflect PLT counts. Notably higher PDW values of the SGA and Oligohydramnios group in both first and third trimester could not be attributed to any specific pathologic mechanism. There are two different studies in the literature about high PDW values; one of them attributed it to having high predictive value to make the diagnosis of threatened preterm labor (16), other one attributed it to having a role as a prediction marker for the severity of preeclampsia (17). Probably, patients diagnosed with SGA and oligohydramnios may share the same pathogenesis which make increase PDW values as threatened preterm labor and preeclampsia. Further studies may clarify this point of view.

No fetal or early neonatal death was observed, probably because we diminished risks by excluding the patients who had foreknown systemic diseases to provide equal standards among groups at the beginning of the study. Because the study is a retrospective, nonrandomized case control study, there are limitations. Scarcity of patients diagnosed with SGA and/or oligohydramnios and without risk factors caused limited sample, especially as in the solely oligohydramnios group.

In conclusion, most leukocyte indices and most platelet indices, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in first or third trimester were not associated with SGA birth and/or oligohydramnios in our study, but it was clarified that they differ significantly between first and third trimester. A new prospective study with larger sample size may present different results. In clinical practice, haematologic variables may not provide a significant benefit in sight, but at least, it may help to clinician in order to assess the patient in a different perspective.

References


