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The association between mean platelet volume and infants with meconium-stained amniotic fluid

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Abstract. – OBJECTIVE: The exact pathophysiology of meconium passage into the amniotic fluid is unknown, but it is frequently associated with fetal hypoxia. The mean platelet volume (MPV) seems to be a marker of platelet production and consumption and may be related to the severity of some diseases associated with bone marrow, hypoxia, and perinatal infections. We aimed to investigate the association between MPV levels and meconium-stained amniotic fluid (MSAF) in infants.

PATIENTS AND METHODS: MPV, serum-reactive protein and hemoglobin levels, and leukocyte and thrombocyte counts were measured in 106 infants with MSAF and a comparison group of 78 healthy control infants.

RESULTS: The mean MPV values of the infants with MSAF were statistically significantly lower than those of the control group ($p < 0.001$). There was no statistically significant difference in the hemoglobin levels or leukocyte and thrombocyte counts in the study group compared to the control group ($p > 0.05$). There was also no statistically significant difference in the MPV levels of the infants with meconium aspiration syndrome (MAS) compared to the infants with MSAF without MAS ($p = 0.107$). The optimal cut-off value for the MPV was 9.90 fl (area under the curve [AUC: 0.788]) in the infants with MSAF, with a sensitivity of 78.1% and specificity of 74.3%.

CONCLUSIONS: Our data suggest that the MPV levels of infants with MSAF were significantly lower than those of healthy infants. This might be associated with a hypoxic process. However, the MPV levels of infants with MSAF and MAS were statistically similar. Thus, the MPV level could not be used to detect patients with or without severe disease.

Key Words:
Mean platelet volume, Meconium-stained amniotic fluid, Meconium aspiration syndrome, Newborn.

Introduction

Meconium-stained amniotic fluid (MSAF) is seen in 7-20% of deliveries, and 5% of infants born with MSAF develop meconium aspiration syndrome (MAS)[1]. Various factors, such as placental insufficiency, intrauterine infections, oligohydramnios, maternal hypertension, or maternal drug abuse (tobacco, cocaine), lead to in utero passage of meconium[2]. The exact pathophysiology of meconium passage into the amniotic fluid is unknown, but it is frequently associated with fetal hypoxia[3]. MAS is a major cause of respiratory morbidity and mortality in term and especially post-term newborns. MAS is defined as respiratory distress in an infant who is born with MSAF[4]. MAS is associated with pulmonary vasoconstriction from hypoxia and substances released during inflammation[5]. Meconium contains a number of substances, such as gastrointestinal mucin, lanugo hair, biliary acids, and free fatty acids. It also contains enzymes, including pancreatic phospholipase A2, as well as proinflammatory interleukins and tumor necrosis factor-α. These substances have the potential to induce dysfunction of pulmonary surfactant and trigger inflammation, which contributes to lung edema[6].

Platelets play a major role in inflammation and fibrin formation[7]. The mean platelet volume (MPV) varies according to the function and activity of platelets[8]. MPV is an important predictor of cardiovascular risk in adults[9]. Studies have reported that MPV is associated with many diseases, such as acute ischemic stroke, familial Mediterranean fever, periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome[10-12].

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MPV has been investigated in neonatal respiratory distress syndrome (RDS) and in preterm infants[13,14].

We hypothesized that fetal hypoxia, which is responsible for the pathophysiology of MSAF, could affect the MPV and that the MPV could be a predictive factor for MSAF. The aim of this study was to compare the MPV levels of infants with MSAF with those of a healthy control group. To our knowledge, there are no published data on this issue.

Patients and Methods

Study Population

This prospective study was conducted at the Neonatology Clinic of Adiyaman University Hospital (a level II Neonatal Intensive Care Unit) in Adiyaman, Turkey, between October 2013 and March 2014. One hundred-six infants with MSAF who had completed more than 37 weeks of gestation (35 of whom had MAS syndrome) were included in the study. Seventy-eight healthy control infants were also prospectively included as a comparison group. Those with MSAF, detected after spontaneous or artificial rupture of membranes, served as cases, and those with clear liquor were used as a control group. The criteria used to confirm the diagnosis of MAS were: respiratory distress (tachypnea, grunting, nasal flaring, retractions, and mild cyanosis) in an infant born with MSAF, roentgenographic findings consistent with MAS (overexpansion of the lungs, with widespread coarse infiltrates), and symptoms that could not be otherwise explained[1]. Infants with hypoglycemia, polycythemia, hypocalcemia, respiratory distress syndrome, congenital malformations, congenital metabolic diseases, congenital pneumonia, sepsis, perinatal asphyxia and infants whose mothers smoked were excluded. The study was approved by the Ethics Committee of Adiyaman University, and informed consent was obtained from all the parents before study entry.

Blood Samples

Blood from both groups was drawn by venipuncture in the first 2 h of life before any feeding, medication, or intravenous fluid infusion. Each sample of whole blood was collected in tubes containing ethylenediaminetetraacetic acid. Blood samples were analyzed within 1 h of collection in EDTA tubes. The Sysmex XT 2000i (Roche Diagnostics GmbH, Mannheim, Germany) automated analyzer was used for complete blood counts. The reference range for MPV was between 7.0 and 11 fl.

Data Acquisition

Clinical data were collected from the patients' record charts. They included gestational age, birth weight, gender, route of delivery, Apgar score at 1 min and at 5 min, parity, age of the mother, maternal diseases during pregnancy (hypertensive disorders, pre-eclampsia, and diabetes mellitus), intrauterine infections, oligohydramnios, maternal smoking, and the severity of MAS (oxygen therapy, application of continuous positive airway pressure therapy, intubation, respiratory and/or metabolic acidosis, and pulmonary hypertension).

Statistical Analysis

Statistical analysis was performed using the Statistical Package of Social Science (SPSS), Version 15.0 (SPSS, Inc., Chicago, IL, USA). Data were expressed as the mean ± standard deviation. A chi-square test was used for the comparison of gender and route of delivery in both groups. An independent two-sample *t*-test was used to compare the birth weight distribution, gestational age and leukocyte, hemoglobin, thrombocyte, and MPV values in the two groups. To determine the optimal cut-off value of MPV measured in MSAF, the receiver operating characteristic (ROC) curve analysis was used. A p value less than 0.05 was considered statistically significant.

Results

One hundred-six infants with MSAF (35 of whom had MAS syndrome) and 78 control infants with no respiratory distress were included in the study.

There were no significant between-group differences in gender, birth weight, gestational age, age of the mother, or maternal diseases (oligohydramnios, hypertensive disorders, and diabetes mellitus) during pregnancy ($p > 0.05$). Parity was significantly lower in the study group compared with the control group ($p < 0.05$). There was a positive correlation between MSAF and a first pregnancy. Forty-nine (46.2%) of the infants were girls, and 57 (53.8%) were boys in the study group, and 34 (43.6%) of the infants were girls, and 44 (56.4%) were boys in the control group. Seventy-six (71.7%) of the infants were

Table I. Characteristics of the study and control groups.

	Infants with MSAF (n=106)	Control group (n=78)	*p* value
Gestational age (week)[a]	40.35 ± 0.9	39.7 ± 0.9	0.326
Birth weight (gram)[a]	3353 ± 542	3201 ± 384	0.352
Gender (female/male)	49/57	34/44	0.423
Age of mother (year)[a]	28.7 ± 4.6	27.8 ± 5.6	0.531
Parity (number)[a]	2.1 ± 1.5	3.2 ± 2.2	**0.024***
Delivery mode (vaginal/caesarian)	76/30	52/26	0.904
Maternal pregnancy diseases n (%)			
Oligohydramnios	3 (2.8)	2 (2.6)	0.914
Hypertensive disorders	7 (6.6)	3 (3.8)	0.412
Diabetes mellitus	8 (7.5)	8 (10.2)	0.402

[a]Values are presented as means ± SD; *$p < 0.05$.

born vaginally, and 30 (28.3%) were born by a cesarean section in the study group. In the control group, 52 (66.7%) of the infants were born vaginally, and 26 (33.3%) were born by a cesarean section (Table I).

There was no statistically significant difference in the hemoglobin levels or leukocyte and thrombocyte counts of the study group compared to those of the control group ($p > 0.05$) (Table II). The mean MPV value of the study group was 9.13 ± 1.26 fl, whereas that of the control group was 10.70±1.27 fl. The mean value of MPV in the study group was statistically significantly lower than in the control group ($p < 0.001$) (Table II). The mean MPV values of the infants with MAS were 8.86 ± 0.98 fl, whereas those of the infants with MSAF but without MAS were 9.42 ± 1.28 fl. There was no statistically significant difference in the MPV levels of the infants with MAS compared to those with MSAF without MAS ($p = 0.107$). Twenty-six infants with MAS (74.3%) were supported with continuous positive airway pressure therapy, and 9 (25.7%) infants were supported with intubation for respiratory distress. No correlation was found between the serum MPV levels and the severity of MAS ($p = 0.356$).

The optimal cut-off value of MPV for infants with MSAF was 9.90 fl (area under the curve [AUC]: 0.788), with a sensitivity of 78.1% and specificity of 74.3% (Figure 1).

Discussion

MPV is widely used to determine thrombocyte function and activity. Large platelets are hemostatically more active[15]. The platelet count has an inverse relationship with MPV because young platelets are larger than older ones. The use of MPV was previously evaluated in the differential diagnosis of hyperdestructive and hypoproductive types of thrombocytopenia[16]. According to some studies, MPV seems to be a marker of platelet production and consumption and may be related to the severity of some diseases associated with bone marrow, hypoxia, and perinatal infections[17-19]. Based on these observations, we hypothesized that fetal hypoxia in infants with MSAF may impair platelet functions. In the present study, we investigated the association between MPV values and MSAF in newborns for the first time.

Table II. Comparison of laboratory parameters between the groups.

	Infants with MSAF (n=106)	Control group (n=78)	*p* value
Leukocyte ($\times 10^9$/L)[a]	19.32 ± 5.35	17.30 ± 5.46	0.487
Hemoglobin (g/dL)[a]	17.19 ± 1.84	18.01 ± 2.31	0.101
Thrombocyte ($\times 10^9$/L)[a]	227.05 ± 86.3	189.33 ± 55.9	0.869
MPV (fl)[a]	9.13 ± 1.26	10.70 ± 1.27	**< 0.001**

[a]Values are presented as means ± SD.

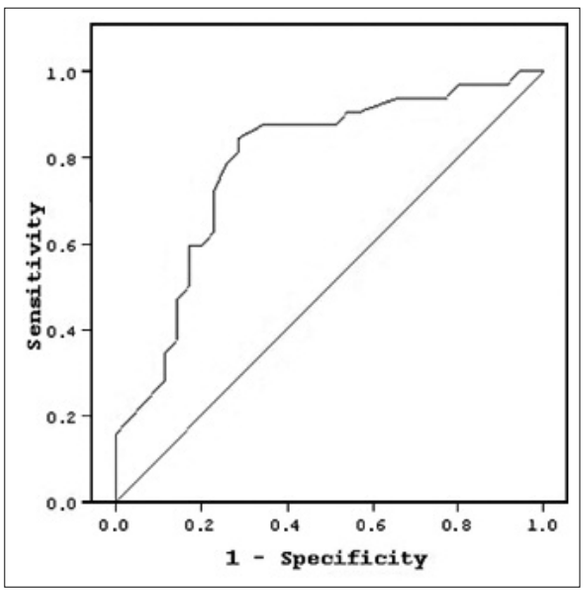

Figure 1. ROC (recevier operating characteristic) curve for the optimal cutoff value of mean platelet volume (MPV).

Some results suggested that the routine measurement of platelet counts and MPV values may be a quick and reliable guide in the assessment of the response of bone marrow to sepsis evolution in infants[19]. However, others could not find any difference between infants with and without sepsis[14]. It has been reported that high levels of MPV were associated with an increased risk of necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), and intraventricular hemorrhage (IVH) in preterm infants[14]. The platelet count was also reported to be an important risk factor in the severity of NEC[20]. Wasiluk et al[21] reported that a decreased blood platelet count, platelet hematocrit, and a large metabolically active platelet count reduced the synthesis and excessive consumption of coagulation factors in hyperclotting in a manner characteristic of intrauterine growth retardation. In the present study, we found that the MPV values of infants with MSAF were significantly lower compared to those of healthy babies ($p < 0.001$), but the platelet counts of the two groups were not different ($p = 0.869$).

Surfactant dysfunction plays a significant role in MAS. MAS is also associated with inflammation, lipid and protein oxidation, and pulmonary vasoconstriction, which may reduce the efficacy of surfactant[22]. It was reported that MPV values were higher in neonates with RDS[13]. In the present study, we found that the MPV values of infants with MAS were significantly lower compared to those of healthy infants. However, the MPV values were not statistically significantly different compared to those with MSAF without MAS ($p \square 0.107$). We supposed that fetal hypoxia might be the main mechanism that affects platelets in infants with MSAF and MAS, and we detected lower MPV values due to decreased platelet functions.

One study reported that a thickened meconium, a low Apgar score (< 7), and acidosis (pH < 7.1) were determinants of MAS development[23]. In our study, the optimal cut-off value of MPV in infants with MSAF was 9.90 fl (AUC: 0.788), with a sensitivity of 78.1% and specificity of 74.3%. We also investigated whether MPV was a predictive marker for the development of MAS. However, the MPV values were statistically similar between MSAF and MAS. Thus, the MPV level could not be used to detect patients with or without severe disease.

Conclusions

The analysis of the MPV is a simple laboratory investigation. In the present study, we demonstrated that the MPV levels of infants with MSAF were significantly lower compared to those of healthy infants. We also illustrated that the MPV is an accurate marker for distinguishing MSAF infants from healthy controls. This might be associated with the hypoxic process. As the MPV levels were statistically similar between MSAF and MAS, they could not be used to detect patients with or without severe disease. Further trials, including large samples, are needed to confirm the results.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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