

# Mean platelet volume in very preterm infants: a predictor of morbidities?

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**Abstract. – BACKGROUND:** Mean platelet volume [MPV] is an important predictor for many diseases and larger platelets are more reactive and associated with shortened bleeding time. Although elevated MPV values are related to respiratory distress syndrome [RDS] in neonates, there are, to our knowledge, no data investigating the relationship between MPV and other diseases of preterm infants.

**AIM:** To assess the correlation between MPV and the occurrence of various morbidities of prematurity such as necrotizing enterocolitis [NEC], bronchopulmonary dysplasia [BPD], sepsis, retinopathy of prematurity [ROP], and intraventricular hemorrhage [IVH] in a cohort of very preterm infants.

**SUBJECTS:** We studied infants with a gestational age of < 34 weeks and a birth weight of < 1500 g admitted to a third level Neonatal Intensive Care Unit. Enrolled infants were divided into NEC and non-NEC, sepsis and non-sepsis, ROP and non-ROP, BPD and non-BPD and IVH and non-IVH groups. MPV was evaluated at birth [cord blood] and repeated at 48-72 hours of life.

**RESULTS:** Two hundred and seventy two infants were studied. MPV measured at birth was similar between sepsis and non-sepsis, and ROP and non-ROP groups. MPV values were higher in infants with BPD [9.08±1.3 fl], IVH [8.4±1.1fl] and NEC [8.6±0.7 fl] when compared to the control group [7.6±0.6 fl] in the first day of life.

**CONCLUSIONS:** High MPV in the first hours of life may reflect the presence of a risk factor for the development of NEC, BPD and IVH in extremely preterm infants. This might be associated with inflammatory and oxidative process. However, our data indicate that higher MPV values are not associated with the development of sepsis or ROP in this study population.

*Key Words:*

Main platelet volume, Respiratory distress syndrome, Neonatal intensive care units.

IVH = IntraVentricular Hemorrhage  
MPV = Mean Platelet Volume  
NEC = Necrotizing Enterocolitis  
NICU = Neonatal Intensive Care Unit  
PDA = Patent Ductus Arteriosus  
RDS = Respiratory Distress Syndrome  
ROP = Retinopathy of Prematurity

## Introduction

Mean platelet volume [MPV] is an important cardiovascular risk predicting factor in adults<sup>1</sup>. MPV has a predictive value for the appearance of stroke and acute myocardial infarction<sup>2</sup>. It is also increased in diabetes<sup>3</sup>, obesity, and rheumatologic and systemic diseases such as psoriasis<sup>4</sup> and familial mediterranean fever<sup>5,6</sup>. MPV has also been investigated in some of the patients with platelet related disorders and an association between maternal MPV and an adverse neonatal outcome has been demonstrated<sup>7</sup>.

Platelet size information is widely and easily available to health care givers as a part of data obtained from complete blood count. Platelets have a main role in fibrin formation and deposition. We also know that platelet counts of infants with sepsis are lower than infants without sepsis<sup>8</sup>. Respiratory distress syndrome [RDS] is one of the most commonly encountered diseases in neonatal intensive care units (NICU) and one of the major causes of mortality and morbidity in preterm infants<sup>9</sup>. In our previous report we found that infants with RDS had higher MPV levels<sup>10</sup>, and our new hypothesis in the present study was whether MPV could be a predictive marker for other relatively frequently encountered diseases in preterm infants as, to our knowledge, there are no data about this issue. In this study we aimed to assess the correlation be-

## Abbreviations

BPD = Bronchopulmonary Dysplasia  
GW = Gestational Age [week]

tween MPV and the occurrence various morbidities of prematurity such as necrotizing enterocolitis [NEC], bronchopulmonary dysplasia [BPD], sepsis, retinopathy of prematurity [ROP], and intraventricular hemorrhage [IVH] in a cohort of very preterm infants.

## Materials and Methods

### Study Population

Infants with birth weights of under 1500 g and 34 weeks of gestation were included in this study. The institutional Ethics Committee approved the study protocol. Written informed consent was obtained from a parent or guardian of each infant. Because infants who die early cannot develop BPD or severe ROP, only infants who survived until at least postnatal 28<sup>th</sup> day of life or 36 weeks' postmenstrual age were eligible for the present study.

### BPD, IVH, and Severe ROP

BPD was defined as the need for supplemental oxygen at postnatal 28th day of life or 36 weeks' postmenstrual age<sup>11,12</sup>. Intraventricular hemorrhage was defined on the basis of ultrasound scans obtained before day 28 of life and was graded from 0 to 4 on the basis previous definitions<sup>13,14</sup>. ROP was diagnosed according to the international classification<sup>15</sup>. Unilateral or bilateral ROP of stages 3, 4 and 5 was considered severe, as was ROP in infants who received cryotherapy or laser therapy in at least 1 eye.

### Sepsis, Meningitis, and NEC

In NICU, we recorded prospectively all episodes of neonatal sepsis and meningitis that were confirmed by the finding of a blood and/or cerebrospinal fluid culture growing bacteria. The decision to obtain blood or cerebrospinal fluid for culture was at the discretion of the NICU clinicians. NEC was a prespecified secondary outcome and diagnosed by a finding of pneumatosis intestinalis, hepatobiliary gas, or free intraperitoneal air on radiography and graded according to modified Bell's criteria<sup>16</sup>.

### Blood Samples

Blood samples were drawn from umbilical cord in the first two hours of life before any feeding, medication and intravenous fluid infusion. On postnatal day 3 [48-72 hours] complete blood count [CBC] was repeated. Blood for CBC was

obtained either by venipuncture, by arterial puncture or through a central catheter. Platelet count and MPV determinations were performed on the Coulter Counter model LH [Coulter Electronics, Hialeah, FL, USA].

### Statistical Analysis

Comparison of parametric data and non-parametric data between groups were done using Student t test and Mann Whitney U test respectively. A *p* value of < 0.05 was considered significant. Results were given as mean and standard deviation. All statistical analysis was carried out using the software Statistical Package for Social Sciences [SPSS Inc. for Windows<sup>®</sup> version 17, Chicago, IL, USA].

## Results

Two hundred and seventy two premature infants were enrolled in the study. Of these 152 infants served as controls because they did not experience any of following diseases: NEC, BPD, sepsis, ROP or IVH. Remaining 120 infants were diagnosed to have at least one of these diseases. BPD was diagnosed in 44 of the infants, 42 infants had IVH, 21 had NEC, 19 had ROP and 33 had sepsis. Thirty nine infants had more than one of these diseases.

The demographic characteristics, platelet counts and sizes of BPD, IVH and NEC groups are shown in Table I.

There were no statistically significant differences between the demographic characteristics of the control and disease groups. MPV was significantly higher in infants with BPD [9.08±1.3 fl], IVH [8.4±1.1fl] and NEC [8.6±0.7 fl] in comparison to the control group [7.6±0.6 fl] in the first day of life [p values are 0.003, 0.0038 and 0.001, respectively]. There were no statistically differences in MPV values between infants with ROP [7.9±0.9 fl] and sepsis [7.8±0.9 fl], and controls [p values are 0.823 and 0.954, respectively]. Comparison of the MPV values of the groups are given in Figure1.

## Discussion

To our knowledge this is the first study which investigates the possible relationship between MPV values and occurrence of BPD, NEC, ROP, sepsis and IVH in very preterm infants.

Table I. Comparison of infants with BPD, IVH and NEC vs controls.

	Infants with BPD (n=44)	Infants with IVH (n=42)	Infants with NEC (n=21)	Controls (n=152)	P <sup>1</sup>	P <sup>2</sup>	P <sup>3</sup>
Gestational age (week)	28.6 ± 2	30.4 ± 2	30 ± 2	30.5 ± 2.0	0.02	0.71	0.25
Birth weight (g)	944 ± 235	1147 ± 225	1105 ± 225	1179 ± 241	0.023	0.59	0.179
Apgar score (5th minute)	7.1 ± 1	7.7 ± 1	7.8 ± 1	8.1 ± 1	0.1	0.1	0.1
Male/female	24/20	23/19	14/7	77/75			
Hemoglobin (g/dl)	14.1 ± 2	14.0 ± 2	13.8 ± 2	13.9 ± 2	0.908	0.76	0.76
Mean platelet volume in 1st day (fl)	9.08 ± 1.3	8.4 ± 1.1	8.6 ± 0.7	7.6 ± 0.6	0.0003*	0.0038*	0.001*
Mean platelet volume in 3rd day (fl)	9.3 ± 1.1	8.9 ± 1.1	9.1 ± 1.2	7.9 ± 0.7	0.004*	0.009*	0.005*
Platelet count in 1st day (/mm <sup>3</sup> )	227.650 ± 96.718	228.811 ± 99.82	207.230 ± 88.32	240.794 ± 97.21	0.052	0.1	0.3
Platelet count in 3rd day (/mm <sup>3</sup> )	176.062 ± 59.265	180.129 ± 77.26	176.420 ± 81.16	199.234 ± 96.12	0.1	0.1	0.2

\*p value is statistically significant, p<sup>1</sup> for BPD vs controls; p<sup>2</sup> for IVH vs controls; p<sup>3</sup> for NEC vs controls.

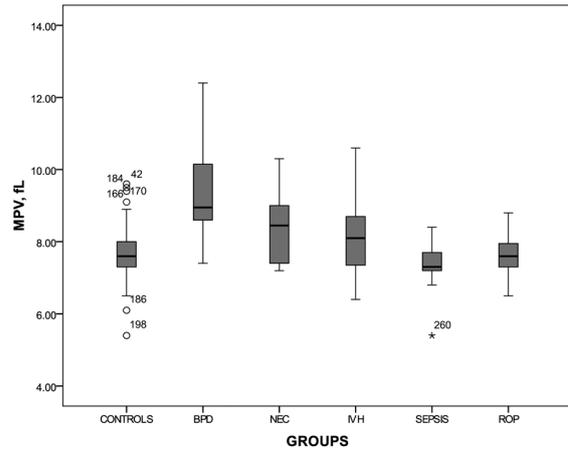


Figure 1. The comparison of MPV values in study groups, lines in blue boxes represent means.

There is an evidence suggesting that MPV may be a predictor of adult coronary and vascular diseases<sup>1</sup>, and we also observed that MPV values were higher in RDS in neonates<sup>10</sup>. In that study there was a relationship between increased coagulation and/or reduced fibrinolysis and fibrin deposition and hyaline membranes in lungs of infants with RDS in whom we found high MPV values<sup>10</sup>.

There are also concerns about the behaviour of platelets and their respective MPV could be an indirect sign of disturbance in platelet production and activity, and bone marrow response in sepsis<sup>17</sup>. Some results suggest that routine measurement of platelet count and MPV may be a quick and reliable guide in the assessment of bone marrow response to sepsis evolution in adults<sup>17</sup>. However, we could not find any difference between infants with sepsis and without sepsis in our study population. This may be due to the complicated and multifactorial etiology of sepsis and also inadequate bone marrow response of preterm infants to infections.

Platelet count is also important as a risk factor for NEC severity<sup>18</sup> and in predicting the type of microorganism in sepsis<sup>8</sup>. Platelet count has an inverse relationship with MPV because young platelets are larger than older ones, and some Authors evaluated the use of MPV in differential diagnosis of hyperdestructive and hypoproduative types of thrombocytopenia<sup>19</sup>. Also the rise of platelet count in association with increased MPV in newborn infants is due to increased production of platelets in the early postnatal weeks<sup>20</sup>. We repeated the measurement of platelet counts on the third day of life to assess the independence of

MPV increase from platelet count. We showed that MPV levels were different between the groups but platelet counts did not change.

MPV seems to be a marker of platelet production, consumption and may be related to severity of some diseases associated with bone marrow, hypoxia, perinatal inflammation and infections. However, it was too interesting that we could not see an increase in MPV in infants with sepsis.

Neonatal diseases such as BPD, NEC, IVH are multifactorial diseases. As a limitation of this study we did not analyze multivariation and demonstration of MPV as an independent risk factor for BPD or NEC. Further analyses are needed to determine of a cut-off value for MPV in very preterm babies.

In conclusion, analysis of MPV and platelet count is a simple laboratory investigation. In this study we found that premature infants with BPD, NEC and IVH had higher MPV levels in early postnatal life than infants without these diseases. This might be associated with inflammatory and oxidative process.

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