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EFFECT OF RESPIRATORY SYNCYTIAL VIRUS INFECTION ON MEAN PLATELET VOLUME IN NEWBORNS

YENİDOĞANLARDA RESPİRATUAR SİNSİTYAL VİRÜS ENFEKSİYONUNUN ORTALAMA TROMBOSİT HACMİ ÜZERİNE ETKİSİ

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ABSTRACT

AIM: To determine the changes in the mean platelet volume (MPV) levels of the babies who were hospitalized in the neonatal intensive care unit due to the respiratory syncytial virus (RSV) infection. It was also aimed to assess whether these changes were related to the severity of the disease, length of hospital stay, and Silverman Anderson respiratory severity score.

MATERIAL AND METHODS: The patients in the study group were formed from the retrospective data of newborn babies at ≥34 weeks of gestation who were hospitalized with the diagnosis of RSV in the neonatal intensive care unit. The control group consisted of healthy newborns without RSV infection. MPV values of the subjects were compared between the groups with and without RSV.

RESULTS: The MPV level in the group with RSV was significantly lower than the control group ($p < 0.05$). No relationship was found between the MPV level of the patients in the RSV group and the number of days of hospitalization, the number of days they received respiratory support, respiratory support need (oxygen, noninvasive and invasive ventilation), hemoglobin levels and Silverman Anderson scoring ($p > 0.05$).

CONCLUSION: We found that infection with RSV in newborns was associated with a decrease in the MPV.

Keywords: *Respiratory syncytial virus; mean platelet volume; Silverman Anderson score*

ÖZET

AMAÇ: Respiratuar sinsityal virüs (RSV) enfeksiyonu nedeniyle yenidoğan yoğun bakım ünitesine yatan bebeklerin ortalama trombosit hacmi (MPV) düzeylerinde meydana gelen değişiklikleri belirlemek ve bu oluşan değişikliklerin hastalığın şiddeti, hastanede yatış süresi ve Silverman Anderson solunum şiddet skorlaması (SAS) ile ilişkisinin olup olmadığını değerlendirmekti.

GEREÇ VE YÖNTEMLER: Çalışma grubundaki hastalar, yenidoğan yoğun bakım ünitesinde RSV tanısıyla yatırılan ≥34 gebelik haftasında yenidoğan bebeklerin retrospektif verilerinden oluşturuldu. Kontrol grubu, RSV enfeksiyonu olmayan sağlıklı yenidoğanlardı. Olguların MPV değerleri RSV olan ve olmayan gruplar arasında karşılaştırıldı.

BULGULAR: Respiratuar sinsityal virus ile enfekte grupta MPV düzeyi, kontrol grubuna göre anlamlı düşük ($p<0.05$) saptandı. RSV grubundaki olguların MPV düzeyi ile hastanede yatış gün sayısı, solunum destek aldıkları gün sayısı, solunum destek ihtiyacı (oksijen, noninvaziv ve invaziv ventilasyon), hemoglobin düzeyleri ve SAS ile arasında bir ilişki saptanmadı ($p>0.05$).

SONUÇ: Yenidoğan bebeklerde RSV ile enfeksiyonun ortalama trombosit hacminin azalması ile ilişkili olduğunu saptadık.

Anahtar Kelimeler: *Respiratuar sinsityal virüsü; ortalama trombosit hacmi; Silverman Anderson skoru*

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INTRODUCTION

Respiratory syncytial virus (RSV) is the most common cause of acute bronchiolitis and viral pneumonia in infants (1). Its prevalence is about 5.2/1000 (26/1000 at age below 1 month). The first six months of the life is a critical period for the severe disease. The rate of hospitalization is three times more common in preterm infants compared to term infants (2). The mortality rate is 2–3% in the neonatal period, 6-7% between one month and one year old, and 1.6% between one and four years old. Although RSV infection is so common, no specific treatment and vaccine has yet been found (3).

Many clinical studies have showed that platelets play an important role in the inflammatory response. Multiple inflammatory factors such as chemokines, cytokines, and coagulation factors are secreted by platelets which increase in size when they are activated. The mean platelet volume (MPV) indicates the size of the platelet, which is associated with platelet function and activation. It is reported that platelet size increases in many disorders and decreases in some. A higher MPV value is indicative of increased platelet activity and therefore more intense inflammation (4, 5). However, MPV decreases in many disorders such as chronic renal failure, acute appendicitis and acute pancreatitis (6). Many studies conducted in the neonatal period investigated a relationship between MPV values and clinical conditions (7).

To our knowledge, there is lack data on the relation between RSV infection and MPV values. Therefore, in this study we evaluated the changes in the MPV levels of newborn patients with RSV. It was also aimed to assess whether these changes were related to the severity of the disease, length of hospital stay, and Silverman Anderson respiratory severity score (SAS) (8).

MATERIALS AND METHODS

The patients in the study group were formed from retrospective data of newborn babies at ≥34 gestational weeks who were hospitalized in the neonatal intensive care unit (NICU) with a diagnosis of lower respiratory tract infection between January 2016 and September 2019 and later diagnosed with RSV.

Ethics committee approval was received for the study from the Keçiören Education and Research Hospital (2012-KAEK-15/2044).

Newborn babies with gestational week <34, SAS missing patients, any syndrome or congenital lung anomaly, chromosome disorder, hematological disorder were excluded. The control group consisted of newborns (at ≥34 weeks of gestation) who applied to the neonatal outpatient clinic but were not diagnosed with any infection or disease. Demographic information, medical history, clinical features, and laboratory results were obtained from the hospital computer records.

Silverman Anderson Respiratory scores were calculated from the clinical data obtained from computer records. SAS were applied to all patients in the study group **(Table 1)**. This score assigns 0, 1, or 2 points depending on the presence and severity of five clinical exam findings: upper chest movement, lower chest retractions, xiphoid retractions, nares dilatation, and expiratory grunting. The score is almost entirely visual and can be performed quickly without expensive equipment, radiography, or laboratory tests, SAS 0 indicated no respiratory distress, 4 -6 indicated moderate respiratory distress and 7-10 indicated severe respiratory distress (8-10). The whole blood count results taken on the first day of hospitalization were evaluated. Platelet count and MPV were determined using a Beckman Coulter hematology analyzer. The reference range for MPV was between 7.7 and 11.2. Platelet mass index (platelet count x MPV) was calculated.

According to our applications, nasopharyngeal aspirates from newborns with clinical sign of respiratory infection were taken within the first 24 hours after admission. Nasopharyngeal aspirates from both nostrils were combined in a standardized manner in NaCl 0.9% without any additives by using a sterile suction trap. Samples for multiplex reverse transcriptase polymerase chain reaction (RT-PCR) testing were stored at +4°C and stored for up to five days. Specimens were tested by RT-PCR in Refik Saydam National Hygiene Center.

Statistical Analyses

SPSS 17.0 (SPSS, Chicago, IL) was used for statistical analysis. The Kolmogorov-Smirnov test was used to determine the distribution of variables. Data are expressed as arithmetic mean ± standard deviation (SD). Differences among two groups were analyzed by student t-test. Chi-square test was performed for

Table 1. The Silverman Andersen Respiratory Severity Score (SAS) evaluates five parameters of work of breathing and assigns an overall score with a patient breathing comfortably a "0" and a patient in severe respiratory distress a "10" (8,18).

FEATURE	Upper chestmovement	Lower chest retractions	Xiphoid retractions	Nares dilatation	Expiratory grunt	Normal ↓ Severe
SCORE 0	Synchronized	None	None	None	None	
SCORE 1	Lag on inspiration	Minimal	Minimal	Minimal	Heard with stethoscope	
SCORE 2	See-saw	Marked	Marked	Marked	Audible	
	Inspiratory				Expiratory	

categorical variables. Pearson test was used to analyze correlation between variables. p values <0.05 were considered statistically significant.

RESULTS

In our study, the MPV level in RSV-infected group was significantly lower (p <0.001), and the platelet count was significantly higher (p=0.002) compared to the control group. The other demographic and laboratory data were similar in groups **(Table 2).** The MPV levels did not correlate with the the number of days newborns stay in NICU, respiratory support need (oxygen, non-invasive and invasive ventilation), the number of days they receive respiratory support and hemoglobin levels (p >0.05). There was a significant negative correlation between the platelet level and MPV of the subjects in the RSV infected group (p <0.001, r = -0.30).

No statistically significant relationship was found between SAS and MPV levels in the RSV infected group (p >0.05). In RSV infected group, SAS was moderately positively correlated to the length of hospital stay (p<0.001, r=0.53). SAS was weakly positively correlated to duration of respiratory support (p=0.002, r=0.33).

We examined the relationship between RSV infection and PMI (Table 2). We found that the PMI was higher in the RSV infected group than the control group. However, this difference was not statistically significant (p >0.05). No statistically significant relationship was found between the PMI level of the patients in the RSV infected group and the number of days of hospitalization, the number of days they received respiratory support, the need for respiratory support and SAS levels (p >0.05). However, the relationship between the PMI levels and hemoglobin levels of the patients in the RSV infected group as statistically significant (p<0.002, r = -0.25).

DISCUSSION

In this study we investigated the changes in MPV levels of infants who were hospitalized in the NICU due to RSV infection and to evaluate whether these changes were related to the severity of the disease, length of hospital stay, and SAS. While MPV level was found to be high in most of the studies (4,11, 12, 13) investigating the relationship between pneumonia and inflammation and MPV, we found that MPV level is low in RSV infection.

Respiratory syncytial virus causes approximately 3 400 000 hospital admissions and at least 66 000 deaths each year, and 99% of these deaths occur in developing countries (14). RSV infections have a serious course especially in high-risk newborns (congenital heart disease, primary and secondary immune deficiencies, bronchopulmonary dysplasia, preterm infants (3, 15).

Platelets play an important role in hemostasis, inflammation, and immune processes. MPV is a routine laboratory test, measured by a whole blood count and seen as a sign of platelet function and activation, and is affected by many inflammatory conditions (16). This means that increased platelet production is accompanied by a decrease in their average volume. In various pathologies, this physiological rate is disturbed (17). Therefore, it is proposed that these parameters are likely to be applied to the diagnosis of certain diseases. Moreover, MPV correlates with platelet activity and is therefore considered a marker of platelet activity (18). It has been reported that a single high MPV measurement is associated with increased morbidity and mortality in various patient populations (11) and high mpv levels were observed in community acquired pneumonia, nosocomial pneumonia and late neonatal pneumonia (12, 13, 19). In contrast, inflammatory conditions involving vascular malformations and intestines are often associated with a decrease in MPV. The mechanism of action of this change is not very understood. It is not known whether the disruption of platelets is involved. However, the most common cause of low MPV is anemia, which is known to cause platelet breakdown. The specific mechanism of the effect of RSV on MPV is unknown (6). Although there is a study in which the prognostic value of MPV was determined in patients with pneumonia (4) as far as we know there are no studies in the literature showing the prognostic value of the MPV in newborn infected with RSV.

In our study, we did not find a significant relationship between the MPV level and the NICU length, and

Table 2. Demographic and laboratory data of the patient and control groups

	RSV Group (n=84) mean±SD	**Control Group** (n=70) mean±SD	***p* value**
Gestation week	37,7±2	37,6±1,2	0.58
Birth weight (g)	3063±559	3209±413	0.07
Postnatal age (day)	20,3±8,9	21,6±5,5	0.28
Hemoglobin (g/dl)	14,1±1,7	14,6±1,5	0.07
Platelet (x10^3/µL)	372±140	311±99	**0.002**
MPV (fL)	8,8±1	9,8±6,3	**<0.001**
PMI (x10^3)	3264±1215	3058±1024	0.26

RSV: Respiratory syncytial virus, MPV: Mean platelet volume, SD: Standard deviation, PMI: Platelet mass index

respiratory support needs of patients. This may due to limited number of patients in our study. As far as we know, all studies with pneumonia have been found to have increased MPV levels (4, 11,12,19, 20). However, Renshaw et al. (6) found that the MPV level decreased in the study of RSV infection in individuals (including children and adults). As part of this study, when they examined MPV levels of patients with other types of viral infections, they could not show a consistent relationship between other viral infections and changes in MPV. Therefore, they stated that the effect of RSV on MPV may be specific to this virus, at least among the common viruses in our hospital. In our study, we found low MPV levels in newborn babies infected with RSV. In centers where RSV diagnostic tests cannot be performed, low rates of MPV may suggest RSV infection in babies presenting to the hospital with lower respiratory tract infection, but more comprehensive studies including viral infections are needed to support this claim.

Globally, many units with device deficiencies use SAS for respiratory failure (8-10). We also used SAS for our patients. We did not find a statistically significant relationship between SAS and MPV level. This may due to limited number of patients in our study. There may be differences in the measurement between the analyzers used to determine the MPV level (13), but our patient and control group patients were studied with the same analyzer. Age-related differences may affect MPV levels (13). To reduce the possible differences due to postnatal age in newborn babies, we made sure that the postnatal ages of the study group and the control group were similar. Since MPV levels may change on different days of the disease, whole blood count data taken on the first day of hospitalization were used in the study. Despite this, our study has some limitations. Since the study was retrospective, we could not reach any data regarding the waiting time of the blood taken for the MPV analysis. Differences in MPV levels can occur due to the increased waiting time before analysis. Besides, the variety of methods used for platelet morphology evaluation is another factor responsible for MPV value differences between laboratories (21).

CONCLUSION

Mean platelet volume is a routine, simple parameter that does not require additional cost or effort during blood morphology by automated hematology analyzers. For this reason, many studies have been conducted to examine the relationship with diseases. While MPV level was found to be high in most of the studies investigating the relationship between respiratory system infection and MPV, we found that MPV level is low in RSV infection and MPV level may be associated with SAS. Low levels of MPV in newborns hospitalized for respiratory tract infections may suggest RSV infection. However, it is necessary to determine the MPV relationship of other infectious agents. However, we think that larger studies are needed to determine the exact role of MPV in newborn infants with RSV infection.

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