Diagnostic Value of the Mean Platelet Volume in the Prediction of Respiratory Syncytial Virus in Acute Bronchiolitis

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ABSTRACT

Aim: Respiratory syncytial virus (RSV) is a viral pathogen that causes lower respiratory system infections in childhood. The purpose of this study was to examine whether mean platelet volume (MPV) changes are significant in the prediction of RSV bronchiolitis.

Materials and Methods: One hundred and eighty-four infants who were diagnosed with acute bronchiolitis were divided into groups based on being RSV positive and other respiratory viruses positive. Using the receiver operating characteristic (ROC), diagnostic accuracy was evaluated according to the areas under the curves (AUC) for the diagnosis of bronchiolitis. A p value of <0.05 was considered statistically significant.

Results: MPV was significantly lower in patients with single RSV (6.6±1.1 vs 7±1.2, p<0.05). The MPVs were similar in patients diagnosed with positive and negative RSV bronchiolitis (6.8±1.5 vs 7±1.3, p>0.05) and other viruses. ROC curve analysis indicates that the MPV level cut-off point for making the diagnosis of single RSV bronchiolitis was 6.63 fL with a sensitity and specificity of 55% and 63% respectively. The median AUC was 0.384 for the MPV (95% CI 0.270-0.499, p=0.04).

Conclusion: Volume of MP may be a useful marker to provide a prediction on single RSV bronchiolitis. However, the measurement of MPV might not be correct and sufficient to provide a prediction on the types of respiratory viruses in bronchiolitis.

Keywords: Mean platelet volume, acute bronchiolitis, respiratory syncytial virus, prediction

Introduction

Respiratory syncytial virus (RSV) is a pathogen that causes lower respiratory system infection in children and infants. RSV associated respiratory infection is a major burden for children and is related with new acute lower respiratory infection episodes in children especially at 5 years of age (1,2). It is the most common etiologic pathogen; however, other viral pathogens such as adenovirus, coronavirus, parainfluenza, influenza, rhinovirus, human metapneumovirus, human bocavirus, and human coronaviruses cause acute bronchiolitis (3,4). Many different medical studies based on different diagnostic and predictive strategies are currently being developed to predict RSV related acute bronchiolitis that is likely to have high mortality and morbidity.

Thrombocytes play an important role in inflammation, allergic reactions, angiogenesis, repair and renewal of tissues through several mediators such as chemokines,

cytokines and coagulation factors. These mediators provide a strong inflammatory response and tissue regeneration. Thrombocytes produced from megakaryocytes in the bone marrow increase their production and also change their volume and distribution range in the bone marrow during any inflammation (5-8). This thrombocyte volume is called mean platelet volume (MPV) in laboratory records. Several studies in recent years have reported that the MPV could be a useful biochemical marker in chronic and/or acute inflammatory diseases (9-12). In a study conducted by Renshaw et al. (12), it was noticed that some patients infected with RSV had relatively low MPVs. However, the clinical importance of MPV in RSV or other virus-related bronchiolitis has not been clearly defined yet.

The aim of this study was to evaluate the changes in MPV on patients diagnosed with RSV related bronchiolitis, to define whether the MPV could be a predictive marker in RSV bronchiolitis, and also to identify whether the type of viral infection affects MPVs in bronchiolitis.

Materials and Methods

Study Patients

One hundred eighty-four patients younger than 24 months (excluding newborns) who were hospitalized with acute bronchiolitis between August 2015 and August 2017 at the General Pediatrics Ward of the Children's Hospital were included in this study. The diagnosis of acute bronchiolitis was based on at least 2 of the following signs: chest retractions, tachypnea, and wheezing or rales on auscultation following viral upper respiratory tract infection in children less than 24 months of age for the first time (13). We excluded those infants who had been hospitalized within a 2-week period prior to the current admission, who developed nosocomial acute bronchiolitis, or who had a known history of any chronic disease. The Local Ethics Committee of Ege University approved this study (approval number: E.155324). Infants who were hospitalized with acute bronchiolitis were recruited with informed, written, parental consent.

Data Acquisition, Blood Samples, and Detection of Respiratory Viruses

The age, gender, clinical findings, values of MP, white blood cell count (WBC), C-reactive protein (CRP), and lymphocyte percentage were recorded from each patient's chart. Complete blood counts were performed on presentation for all patients using a commercially available analyzer [CELL-DYN Ruby, Abbott Park, Illinois, United States of America (USA)].

A nasal smear was obtained from each infant and tested for the presence of RSV, influenza virus types A and B, adenovirus, parainfluenza viruses, human rhinovirus, human coronavirus, human metapneumovirus, and human bocavirus with multiplex reverse-transcription polymerase chain reaction (PCR) methods (RealAccurate, Respiratory RT PCR, PathoFinder, Netherlands, and Seeplex RV15 ACE Detection, Seegene, South Korea). Nasal samples were obtained more commonly by a nurse or sometimes a research assistant on all subjects within 48 hours of admission using a standardized protocol (14). Samples were frozen at -20 °C and transported in ice to the department of clinical microbiology and virology laboratory of our university for viral nucleic acid amplification.

Statistical Analysis

Statistical analyses were performed using IBM SPSS version 21.0 for personal computers (Chicago, IL, USA). The categorical variables were analyzed using the Fisher's exact test group if there were different groups. The Mann-Whitney U test was used to analyze non-normally distributed data. As for the receiver operating characteristic (ROC) curves for the biomarkers, calculation of their sensitivity and specificity in acute bronchiolitis was evaluated by drawing the discriminative ability of MPV in respiratory viruses. A value of $p<0.05$ was considered as statistically significant.

Results

In this study, the population included 184 children with acute bronchiolitis. One hundred and fourteen (62%) of them were male, and 70 (38%) were female. The median age was 12±14.5 months. One hundred and twenty-six (68.5%) children had at least one viral respiratory agent and the most common two viruses were RSV (18%; n=51) and rhinovirus (16.2%; n=46). The distribution of respiratory viruses is shown in Figure 1. RSV was the most common agent. The MPVs were similar in patients with positive
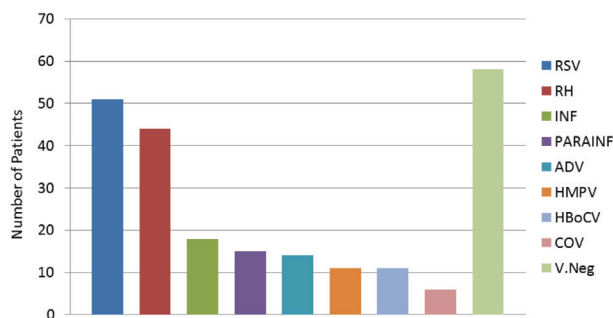

Figure 1. Distribution of respiratory viruses
RSV: Respiratory syncytial virus, RH: Rhinovirus, INF: Influenza virus, PARAINF: Parainfluenza virus, ADV: Adenovirus, HMPV: Human metapneumonia, HBoV: Human bocavirus, COV: Coronavirus, V. Neg: Virus negative

and negative RSV bronchiolitis (6.8±1.5 vs 7±1.3, p>0.05). The comparison of the lymphocyte percentage showed a significantly higher lymphocyte percentage in infants with RSV bronchiolitis (p<0.05).

The differences that were found regarding the laboratory findings between patient groups with respiratory viruses are given in Table I. The MPV was significantly lower in patients with single RSV bronchiolitis versus their negative counterparts (6.6±1.1 vs 7±1.2, p=0.04). The groups who had non-single RSV bronchiolitis tended to possess a statistically significant higher WBC (p=0.02). Being positive or negative in terms of respiratory viruses did not make any statistical difference in MPV and other laboratory findings.

ROC curve analysis indicated that the cut-off of MPV level point for making the diagnosis of single RSV bronchiolitis was 6.63 fL with sensitivity and specificity of 55% and 63% respectively. The AUC value of MPV was lower than WBC, CRP and lymphocyte (Table II and Figure 2).
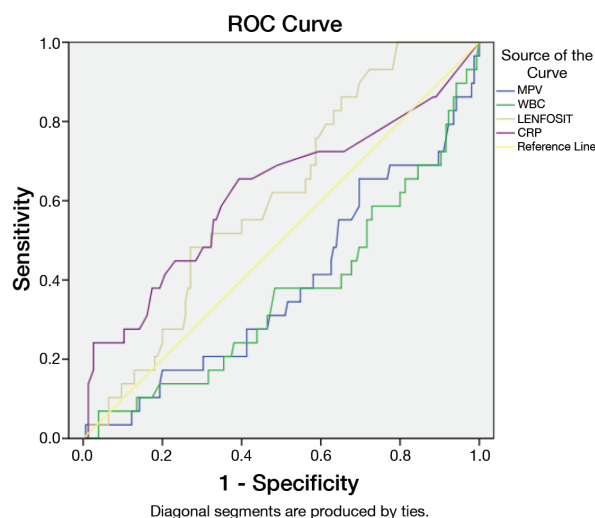

Figure 2. Receiver operating characteristic curve of mean platelet volume, white blood cell, and C-reactive protein count for single respiratory syncytial virus bronchiolitis

MPV: Mean platelet volume, WBC: White blood cell, CRP: C-reactive protein, ROC: Receiver operating characteristic, RSV: Respiratory syncytial virus

Table I. Comparison of laboratory data of patients in terms of respiratory virus groups					
Viruses	**MPV (med ± IR) (f/L)**	**WBC (med ± IR)/mm³**	**Lymphocyte (med ± IR) (%)**	**CRP (med ± IR) (mg/dL)**	**p value**
RSV					
Single, (n=29) Non-single, (n=97)	6.6±1.1 7±1.2	8960±6420 11760±6540	51±30 37.9±37	0.9±4.3 0.3±1.2	[a]0.04, [b]0.02, [c]NS, [d]0.04
Rhinovirus					
Positive, (n=46) Negative, (n=28)	7±1.2 6.8±1.3	12690±6602 1100±5110	29±31.2 44±30	0.3±1.6 0.6±1.9	[a]NS, [b]NS [c]0.01, [d]NS
Adenovirus					
Positive, (n=18) Negative, (n=60)	7±0.9 6.9±1.4	11900±6375 11220±6092	41±50.5 40.4±34.2	0.5±1.4 0.4±1.7	[a]NS, [b]0.03 [c]NS, [d]NS
Virus					
Positive, (n=136) Negative, (n=58)	6.9±1.3 6.9±1	11300±5300 12300±7500	40±37 35±34	0.4±1.7 0.3±1	[a]NS, [b]NS [c]NS, [d]NS

MPV: Mean Platelet Volume, WBC: White Blood Cell, CRP: C-reactive protein, RSV: Respiratory Syncytial Virus, NS: Not significant, [a]: shows the statistical difference of MPV in virus groups, [b]: shows the statistical difference of WBC in virus groups, [c]: shows the statistical difference of lymphocyte percentage in virus groups, [d]: shows the statistical difference of CRP in virus groups

Table II. Results of the receiver operating characteristic curve of mean platelet volume, C-reactive protein, white blood cell and lymphocyte for single respiratory syncytial virus bronchiolitis				
Variable	**Area under the curve**	**Standard error**	**p value**	**95% CI**
MPV	0.384	0.059	0.04	0.270-0.499
CRP	0.364	0.059	0.02	0.249-0.479
WBC	0.608	0.051	0.06	0.509-0.778
Lymphocyte	0.620	0.064	0.04	0.494-0.745

MPV: mean platelet volume, CRP: C-reactive protein, WBC: White blood cell, CI: Confidence Interval, p value of <0.05 was considered statistically significant

Discussion

Our current study of the infants hospitalized with bronchiolitis has shown that the respiratory pathogens which cause acute bronchiolitis cannot be diagnosed or predicted by MPV. Our results indicated that bronchiolitis with RSV is associated with a reduced MPV which was not statistically significant. However, we demonstrated that a single RSV had lower MPV compared to a non-single RSV bronchiolitis with an MPV under 6.63 fL that was relatively sensitive and specific for the single RSV infection. Other studies that investigated the differences of the laboratory markers of acute bronchiolitis have demonstrated a negative correlation between MPV and acute bronchiolitis (11,12). Similar to our study, Renshaw et al. (12) reported that MPV was lower in patients hospitalized with RSV compared to a control group by rapid RSV assays and viral cultures in 158 patients, 112 of which were aged <18 years. In this study, it is also reported that the MPV under 8.9 fL with a sensitivity of 71% and specificity of 49% is a useful marker for RSV bronchiolitis in children undergoing bronchoscopy.

A systematic review of the current literature for studies concerning MPV and pediatrics, published up to 2017 in databases such as Pubmed using search terms including "MPV", "pediatrics", to identify reports that presented data on these topics was carried out. In Pubmed, more than 100 articles were identified. However, the topics of MPV, pediatrics and acute bronchiolitis combined were found in only one article (11). Although the MPV measurements in autoimmune, cardiac conditions and most infections were reported in adult studies, there is a lack of information on MPV for pediatric patients with acute bronchiolitis diagnosed with RSV or other respiratory viruses.

Actually, the current study into changes of MPV has proved that there is no relationship between respiratory viruses and MPV. However, infants with single RSV bronchiolitis have significantly decreased MPVs compared to those with RSV accompanied by other respiratory viruses in our study. Thus, we suggest that the impact of single RSV on MPV might be specific to this virus condition and MPV may be a useful predictor for diagnosing single RSV bronchiolitis.

Study Limitations

There are several limitations to this study. We only investigated hospitalized patients with acute bronchiolitis, and not those infants who applied to the emergency services or out-patients policlinics, so our study group was limited. Prospective studies with a larger number of patients are needed to assess the role of MPV values in acute bronchiolitis.

Conclusion

MPV may be utilized for the diagnosis of single RSV bronchiolitis. However, we think that MPV is not a reliable marker in specifying the cause of acute bronchiolitis; and that its diagnosis could simply be made by conventional microbiological methods. Rather than guessing the virus type according to laboratory findings, we should use more accurate diagnosis methods that will allow for treatment.

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