



DOI: 10.5137/1019-5149.JTN.16659-15.1

Received: 27.11.2015 / Accepted: 25.1.2016

Published Online: 13.04.2016

Original Investigation

# Platelet Indices in the Diagnosis of Ventriculoperitoneal Shunt Infection in Children

Umit CELİK<sup>1</sup>, Tamer CELİK<sup>2</sup>, Orkun TOLUNAY<sup>3</sup>, Cigdem DONMEZER<sup>3</sup>, Yurdal GEZERCAN<sup>4</sup>, Kurthan MERT<sup>3</sup>, Ali Ihsan OKTEN<sup>4</sup>

<sup>1</sup>Adana Numune Research and Training Hospital, Department of Pediatric Infection, Adana, Turkey

<sup>2</sup>Adana Numune Research and Training Hospital, Department of Pediatric Neurology, Adana, Turkey

<sup>3</sup>Adana Numune Research and Training Hospital, Department of Pediatrics, Adana, Turkey

<sup>4</sup>Adana Numune Research and Training Hospital, Department of Neurosurgery, Adana, Turkey

## ABSTRACT

**AIM:** Ventriculoperitoneal shunt infection (VPSI) is one of the main causes of mortality and morbidity in hydrocephalus. Platelet indices, mean platelet volume (MPV) and platelet distribution width (PDW) have been evaluated for some infectious diseases. In this study we aimed to investigate whether MPV and PDW values are decisive for the diagnosis of VPSI in children.

**MATERIAL and METHODS:** Charts of VPSI from 2012 to 2015 were reviewed retrospectively. Twenty-five ventriculoperitoneal shunt infected patients and 25 healthy children as the control group were included in the study. Platelet indices were recorded.

**RESULTS:** A total of 25 VPSI patients and 25 healthy children were enrolled in the study. Significant differences were detected between the MPV and PDW values in the two groups ( $p < 0.001$ ). ROC curve analysis suggested a cut off point for MPV as below 9.2 fl (smaller values indicate patients) for the diagnosis of VPSI, with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 80%, 92%, 91% and 82%, respectively. For PDW, the cut-off point was 12.25 (larger values indicate pathology) for diagnosis of VPSI, with sensitivity, specificity, PPV and NPV of 68%, 80%, 77% and 71%, respectively.

**CONCLUSION:** Our results suggest that MPV and PDW can be used for the diagnosis of VPSI in children with an accuracy of at least 75%. Moreover, MPV's specificity is higher than the other platelet parameters and leucocyte count.

**KEYWORDS:** Ventriculoperitoneal shunt infection, Platelet indices, MPV, PDW

## INTRODUCTION

The ventriculoperitoneal shunt has been a main treatment option for hydrocephalus. Ventriculoperitoneal shunt infection (VPSI) is the most common instrument-related complication in hydrocephalus patients, being an important cause of mortality and morbidity (7). Early diagnosis and management are important since pediatric patients may present with non-specific symptoms mimicking other infections. As in the initial phase, shunt infection may not appear with neurological symptoms, and it can be difficult to diagnose (3). Besides clinical findings, cerebrospinal fluid (CSF) analysis (white blood cell, glucose and protein concentrations) with cerebrospinal fluid culture positivity is

essential for diagnosis, as growing the causative agent in the culture or making a diagnosis by using infection indices is not always easy. Moreover, benefits of white blood cell (WBC) counts, C-reactive protein (CRP) and procalcitonin are limited although these markers support the diagnosis of bacterial infection.

Platelet and platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW) are parameters that can be easily examined through blood count. Recent years have witnessed the increase in the number of studies that investigate whether platelet indices may play a role in some infectious and inflammatory diseases and may be used as markers (5,6,8,14,17-19,23).



Corresponding author: Umit ÇELİK

E-mail: ucelik32@gmail.com

To our knowledge, there are no studies conducted examining the diagnosis of VPSI using platelet indices. In this study, we aimed to investigate whether MPV and PDW values are decisive for the diagnosis of VPSI in children.

## ■ MATERIAL and METHODS

### Patients and Study Design

The study was approved by the local ethics committee (Approval number: 193). It was conducted in a tertiary training and research hospital. From 2012 to 2015, all patients diagnosed with proven VP shunt infections were evaluated and included in the study. Patients' medical records were examined retrospectively. During the study period, a total of 25 patients with VP shunt infections were included.

Shunt infection diagnosis of the patients was made by a Pediatric Infectious Disease specialist. All of the other possible infection causes were excluded with a detailed history, clinical physical examination and laboratory evaluation.

CSF for analysis (glucose, protein, culture, WBC count with differential, gram stain) was obtained from the ventriculoperitoneal shunt before antibiotic administration. When CSF glucose, protein values and WBC count with differential were consistent with bacterial infection, proper antibiotic treatment was started. When VPSI was diagnosed, the shunt was removed and external drainage was inserted.

Microorganism was grown in the cerebrospinal fluid of each patient.

The microorganisms that were grown in the CSF were as follows: *Coagulase negative Staphylococcus* (CoNS) 68% (17 patients), *Pseudomonas aeruginosa* 8% (2 patients), *Acinetobacter baumannii* in 12% (3 patients), *Klebsiella pneumoniae* 8% (2 patients), and *Pseudomonas aeruginosa+Klebsiella pneumoniae* 4% (1 patient).

The control group was selected from healthy children who presented to the outpatient clinic. None of them had infectious or chronic diseases.

The complete blood counts (CBC) had been performed on the first day of admission before antibiotic administration and comprised platelet (PLT) counts, MPV, PDW and WBC counts.

### Statistical Analysis

Statistical analysis was performed using the IBM SPSS Statistics Version 20 statistical software package. Categorical variables were provided as numbers and percentages, numerical variables were given as mean±standard deviation. Platelet indices were found to be statistically different between groups, and they were analyzed for diagnostic value in VPSI using Receiver Operating Characteristic (ROC) curve analysis. The areas under the ROC curves (AUC) were calculated and the specificity, sensitivity, positive-predictive value (PPV), negative predictive value (NPV) as well as the accuracy for the platelet, MPV and PDW of the most appropriate cut-off point were calculated for VPSI. p value <0.05 was considered statistically significant.

## ■ RESULTS

Twenty-five VPSI patients and 25 healthy children as the control group were included in the study. Within the patients with VPSI, 6 (24%) were female, 19 (76%) were male and mean age was 11.16±17.13 months. In the control group, 14 (54%) patients were female, 11 male (46%) and their mean age was 8.72±5.42 months. There was no difference in gender distribution and mean age between the control group and the VPSI patients (p>0.05).

The patient group had a mean MPV of 7.78±1.59 fl, and the control group 10.02±0.649 fl. There were significant differences in the MPV values between the two groups (p<0.001). MPV values were significantly lower than in the control group. The mean PDW values of the patient and control group were 14.558±3.635 and 11.612±1.319, respectively. The PDW values were significantly higher in the VPSI group (p<0.001). The mean platelet counts of the patient and control group were 570.12±238.48 mm<sup>3</sup> and 348.32±70.551 mm<sup>3</sup>, respectively. The platelet counts were significantly higher in the VPSI group (p<0.001). The mean white blood cell counts of the patient and control group were 15.67±7.41 mm<sup>3</sup> and 9.43±2.72 mm<sup>3</sup>, respectively. The WBC counts were significantly higher in the VPSI group (p<0.001) (Table I).

A ROC curve was plotted to identify the parameters that may be statistically significant in VPSI. For MPV, the calculated area under the curve was 89.8%. When the MPV value was below 9.2 fl, sensitivity and specificity were 80% and 92%, and PPV and NPV were 91% and 82% respectively (Table II, Figure 1). For PDW value, the area under the curve was 71% and cut-off value was higher than 12.25, sensitivity and specificity were 68% and 80%, and PPV and NPV were 77%, 71%, respectively (Table II, Figure 2). On the other hand, platelet count was higher than 401.500 mm<sup>3</sup>, sensitivity and specificity were 80% and 88%, respectively (Table II, Figure 2). The area under the curve was 77.4% for WBC count and cut off value was higher than 9.73x10<sup>3</sup>/UL, sensitivity and specificity were 76% and 64%, and PPV and NPV were 68% and 73%, respectively (Table II, Figure 2).

## ■ DISCUSSION

Shunt infection is a common cause of mortality and morbidity in patients with hydrocephalus and incidence is reported between 5-15% in literature (16). Especially paediatric patients may apply with diseases mimicking nonspecific findings of other childhood diseases, making early diagnosis vital. Ventriculoperitoneal shunt infection can be seen in functional shunts and may also occur as an important cause of shunt dysfunction. Therefore, early diagnosis and management are important. Although some diagnostic criteria are used, in most cases diagnosis during childhood may not be easy. CSF analysis (protein, glucose, WBC count) provides the warning signs for VPSI. It is often necessary to await CSF culture results.

Platelets play a basic role in hemostasis and thrombosis (21). Platelet indices are parameters that can be easily examined through blood count. Mean platelet volume has been used since the 1970s (11). Platelet indices based on MPV and PDW

have been emphasized in recent years with respect to some infections and inflammatory conditions (5,6,14,17-19,23). The mean platelet volume shows the average size of platelets and platelet production rate and stimulation (4).

It has been demonstrated in recent years that increased MPV is a risk factor associated with the prognosis of cardiovascular and cerebrovascular diseases (1,10). Moreover, MPV was also evaluated in infectious diseases and it was shown that reduced MPV levels were seen in acute appendicitis, respiratory syncytial virus, and HIV infection in the literature (5,17,18). Within the sepsis studies, there are also different results. Some authors associated poor prognosis with increased MPV levels in sepsis while Bessman and Gardner reported reduced MPV levels in septic patients (2,20). Guclu et al. showed that in patients with severe sepsis, PDW and MPV levels were higher

than non-severe sepsis (8). On the other hand, Gunluoglu et al. found lower MPV levels in active pulmonary tuberculosis cases but this did not reflect the severity of disease (9).

Platelets also play an important role in inflammatory response. In the literature, lower MPV levels were correlated with increased disease activity in inflammatory diseases such as ulcerative colitis (23). It is thought that the reason of lower MPV levels observed in inflammatory bowel diseases could be the presence of a defect in the regulation of thrombopoiesis (13).

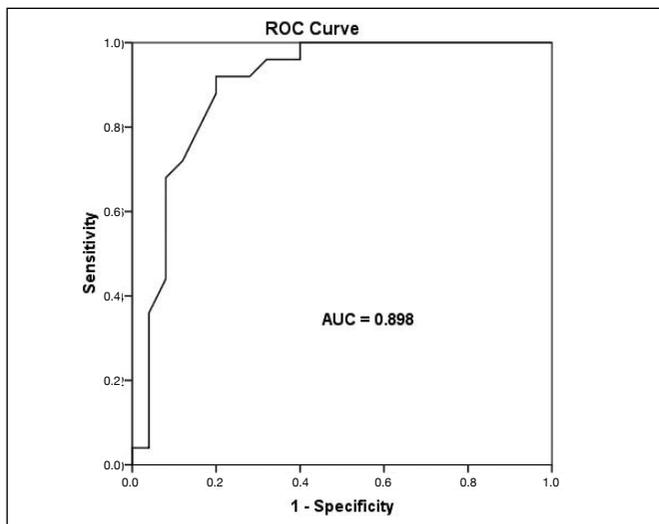
Platelet indices were also evaluated in central nervous system events. Mean platelet volume and PDW were higher in patients with cerebral venous sinus thrombosis with brain parenchymal lesions and predict the severity of thrombosis (12). Also, mean

**Table I:** Laboratory Values of Patients with VPSI and Control

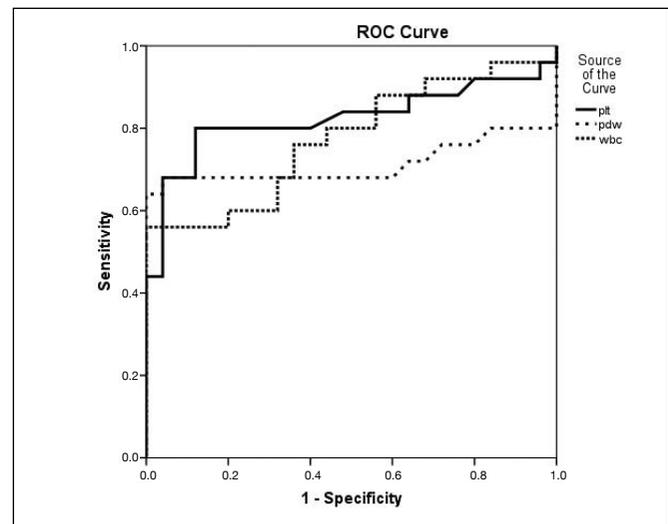
Characteristics	Patient group n=25 mean±SD	Control group n=25 mean ±SD	p-value
MPV (fl)	7.78±1.59	10,02±0,649	<0.001
PDW (%)	14.558±3.635	11.612±1.319	<0.001
Platelet count (mm <sup>3</sup> )	570.12±238.48	348.32±70.551	<0.001
White blood cell (mm <sup>3</sup> )	15.67±7.41	9.43±2.72	<0.001

**Table II:** Results of ROC Analysis for Markers in Predicting VPSI Compared to Control

	Cut-off point	Sensitivity	Specificity	PPV	NPV	AUC	Asymptomatic 95% Confidence Interval Lower/Upper Bound
MPV (fl)	<9.2	80	92	91	82	0.898	0.803/0.992
PDW %	>12.25	68	80	77	71	0.713	0.545/0.880
Platelets (mm <sup>3</sup> )	>401.5	80	88	87	82	0.823	0.694/0.952
White blood cell (mm <sup>3</sup> )	>9.73	76	64	68	73	0.774	0.642/0.907



**Figure 1:** Receiver operating characteristic (ROC) curve for MPV.



**Figure 2:** Receiver operating characteristic (ROC) curve for platelet counts, platelet distribution width and white blood cell counts.

platelet volume has been shown to be an independent risk factor for ischemic stroke (15).

Platelet distribution width (PDW), being another platelet index, indicates heterogeneity in platelet sizes. Increased PDW levels indicate increased platelet distribution that is associated with swelling, destruction and immaturity (6). An experimental study suggests that increased PDW levels were associated with endotoxemia (22). Sepsis studies showed that elevated PDW was related to higher mortality outcomes (6,8).

As a result of this study, we saw that platelet indices, especially MPV, are important parameters in patients with VPSI. Mean platelet volume levels were reduced while PDW and platelet levels were increased compared to the control group in patients with VPSI. This study indicated that MPV and PDW values may be used for the diagnosis of VPSI in children with an accuracy of at least 75%. Our findings indicated that MPV levels lower than 9.2 fl have good (80%) sensitivity and good (92%) specificity for VPSI diagnosis. MPV's sensitivity and specificity are higher than the other platelet parameters and leucocyte count. Therefore, MPV may be used as an ancillary test in the diagnosis of VPSI.

## ■ CONCLUSION

To the best of our knowledge, this is the first study to evaluate MPV and PDW in the context of VPSI diagnosis. Mean platelet volume and PDW values would serve as useful parameters for the diagnosis of VPSI that has a high mortality and morbidity rate. We think that clinicians should be aware of this association.

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