

# EFFECTIVENESS OF COMPLETE BLOOD COUNT PARAMETERS FOR PREDICTING INTRACRANIAL INJURY IN CHILDREN WITH MINOR HEAD TRAUMA

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**Abstract: Objective:** We aimed to investigate the relationship between trauma severity and platelet indices (PI) and white blood cell (WBC) count to identify traumatic brain injury (TBI) in children with minor head trauma (MHT). **Materials and methods:** This prospective study included children with acute isolated MHT who underwent head computed tomography (CT) based on Pediatric Emergency Care Research Network (PECARN) criteria. Mean platelet volume (MPV), platelet distribution width (PDW), MPV to platelet ratio (MPV/PL), MPV to white blood cell ratio (MPV/WBC), and MPV to Neutrophil ratio (MPV/Neu) were evaluated.

**Results:** 86 children with MHT and 245 controls were included the study. WBC, Neu count, MPV, MPV/WBC, MPV/Neu and MPV/PI ratios were statistically different among patients with abnormal CT, patients with normal CT and healthy controls ( $p < 0.05$ ). For predicting abbreviated injury score (AIS)  $> 1$ , the AUC values of WBC, neutrophil, MPV/WBC and MPV/Neu were 0.746, 0.739, 0.726 and 0.724, respectively.

**Conclusion:** In children with MHT who underwent CT, WBC, Neu counts, MPV/WBC and MPV/Neu ratios may be helpful for predicting the severity of trauma in pediatric emergency department.

**Key words:** children; complete blood count; head trauma; intracranial injury.

## INTRODUCTION

Isolated minor head trauma (MHT) is a common cause of presentation at the paediatric emergency room, and includes the majority of all head trauma patients admitted to the paediatric emergency service. The most important mission of the clinician in the management of patients with MHT is to detect serious trauma-

tic brain injury (TBI), which is estimated to represent one-third of all injury-related deaths (1). The most appropriate imaging technique for diagnosing TBI is head computed tomography (CT). Significant TBI is detected in  $< 1\%$  of patients with MHT (1). In clinical practice we use The Paediatric Emergency Care Applied Research Network (PECARN) validated rule to identify children with MHT at very low risk for significant TBI without a head CT scan (2). Nevertheless, paediatric emergency physicians frequently face difficulties making a decision due to exaggerated concerns and insistent attitudes of parents, and usually disagree with neurosurgeons about requests for control head CT scans to detect possible TBI. While an unnecessary CT scan can lead to excessive radiation exposure and costs, bypassing a CT scan despite the insistence of the family may result in missing TBI.

Trauma acts as the trigger for a cascade of hemodynamic, metabolic, neuroendocrine, and immune responses leading to secondary tissue damage (3). Platelets, neutrophils, and lymphocytes are markers that reflect the inflammatory response which is required for subsequent restoration of homeostasis (4). Platelet count and platelet function are predictors of mortality, and the latter also contributes to detrimental cerebral bleeding in TBI (5, 6). The platelet volume indices (PVI) including mean platelet volume (MPV) and platelet distribution width (PDW) reflect the average size of platelets in the blood and correlate with platelet activity and function (7). These are parameters that can be derived inexpensively from a complete blood count (CBC). PVI and MPV have potential clinical utility, particularly in haematology and cardiovascular medicine (8, 9, 10). Until now, the diagnostic performance of MPV, WBC, and platelet count for determining trauma-

ma severity and to identify TBI in patients with MHT have been investigated in few adult clinical studies (11, 12, 13).

To the best of our knowledge, no study has investigated CBC parameters in children with MHT; thus, we determined whether PVI and WBC count could be used as predictors of TBI in those patients. We researched how neutrophils, lymphocytes, platelets, and the PVI derived from a CBC result in changes in children with MHT; and if these parameters are useful to predict TBI.

## MATERIAL AND METHODS

This prospective study was performed in patients with MHT who were admitted to the paediatric emergency and trauma centre of our university hospital between March and July 2017 with approval of the Ethical Committee of Katip Çelebi University. Patients with MHT were characterized as having a Glasgow Coma Score (GCS) of 14 or 15, no abnormal findings on a neurological examination, and no signs of basilar skull fracture such as hemotympanum, oto- or rhinorrhoea, or a periocular or posterior auricular hematoma. The management of all patients and the head CT scan requirements were determined according to the PECARN guidelines. Unenhanced CT scans were performed on a 16-slice MX16 (Philips Medical Systems, Best, Netherlands) scanner with 1.5 mm slices of the cranial base and 2.5 mm for the brain parenchyma. Blood samples were drawn from every patient meeting the study criteria and who were willing to participate in the study within 10 min after they arrived in the emergency room. All head CT scans were evaluated by a neurosurgeon and a radiologist. The presence of a skull fracture (linear or depressed), acute epidural, subdural or parenchymal hematomas, subarachnoid haemorrhage, concussion, and cerebral oedema were considered positive CT results. Severe trauma was defined clinically by any of the following: admission to a ward for at least 48 h, admission to a paediatric intensive care unit (PICU), patients needing intubation, increased intracranial pressure treatment, transfusion, and exitus. Intracranial injury in a CT-positive patient was assessed using the abbreviated injury score (AIS, 2005) and ranked on a scale of 1 to 6, with 1 being minor and 6 being non survivable injury. The patient clinical and demographic characteristics (age, sex, vomiting, duration of loss of consciousness, presence of seizure or focal neurological deficit, presence of scalp hematoma and size, mechanism of trauma, and short outcome) were recorded. Patients whose GCS was < 14; those who had multiple trauma, penetrating injuries, anaemia, chronic disease, acute or chronic infection, bleeding diathesis, soft tissue injury; and patients who were admitted 24 h

after trauma were not included in the study. Eventually, 86 children with acute isolated MHT who underwent a head CT scan and presented to the paediatric emergency room were included in the study. The control group consisted of 245 healthy children who had no trauma, no soft tissue injury, and no infection history during the 3 months before admission for a CBC exam. Written informed consent was obtained from the guardians of each patient before blood was taken.

CBCs were performed using a Coulter analyser (LH-780; Beckman Coulter, Brea, CA, USA) with the impedance method (intra-assay variation coefficient 1.6%, interassay variation coefficient 1.65%), which was routinely checked every month in the central laboratory of our hospital. Standard tubes with a constant amount of K3-EDTA were used. Blood samples of each patient were examined within 15 min to avoid any possible variation in the PVI. The PVI included MPV, PDW, and plateletcrit. Furthermore, we examined other platelet indices calculated based on CBC: MPV/platelets (MPV/PL), MPV/WBC (MPV/W), and MPV/Neu (MPV/N).

The statistical analyses were performed with SPSS for Windows software (SPSS Inc., Chicago, IL, USA). Quantitative data are presented as median with interquartile range. The Kruskal–Wallis test was used to evaluate the differences between study groups (head CT-positive and CT-negative) and healthy group for continuous variables. Differences in the means of continuous variables between groups (head CT-positive and head CT-negative) were analysed with the Mann–Whitney *U*-test. Differences in categorical variables were analysed with the chi-square test. Spearman's correlation test was used to assess the associations between laboratory parameters and the AIS score. The predictive ability of the laboratory data for the trauma severity was evaluated with receiver operating characteristic analyses. A *p*-value < 0.05 was considered statistically significant.

## RESULTS

Of the 86 patients with MHT who underwent a head CT scan based on the PECARN criteria, 27 females (31.7%) and 59 males (68.6%) were included in the study. The median age of the patients with MHT was 3 years (1 month to 17 years). The median age of the control group was 6 years (1 month to 17 years) (*p* > 0.05). A total of 8 patients (9.3%) were injured by in-car accidents, 2 (2.3%) were injured by out-of-car accidents, 26 (30.2%) were injured by falling from a height, 1 (1.1%) was injured by a motor vehicle accident, and 49 (56.9%) were injured by low-energy impact. Sixty patients (69.7%) were discharged after emergency service observation, and eighteen (20.9%) were admitted to

the neurosurgery clinic after initial treatment. Five patients (5.8%) included in the study were in need of surgery, three patients (3.4%) were in need of the PICU, and no patients died.

The evaluation of the head CT scans showed that 36 patients (41.9%) had brain pathologies including skull fractures, whereas the head CT scans of 50 patients (58.1%) were normal. Among the head CT scan-positive group, 20 had isolated skull fractures, 18 of which were linear and 2 that were depressed fractures. Thirteen patients (15.1%) had intracranial haemorrhages (subdural or epidural hematomas). Of these patients, six had a linear skull fracture and one had a depressed skull fracture. Three of the patients (3.5%) had contusions with a linear skull fracture on a head CT scan. The clinical and demographic characteristics of the patients are shown in Table 1.

When we divided the cases into three groups based on the presence or absence on head CT scans and the control group, we found that WBC, Neu, MPV, MPV/PL, MPV/W, and MPV/N were significant variables (Table 2).

The WBC and Neu values increased progressively from the healthy controls (8.5/L and 3.3/L) to head CT-negative patients with MHT (10.4/L and 4.7/L), and further to patients with a head CT-positive scan (12.2/L and 7.1/L;  $p < 0.01$ ). The MPV/W and MPV/N values decreased progressively from the healthy controls (1 and 2.5) to head CT-negative patients (0.74 and 1.5), and further to head CT-positive patients (0.64 and 1.16;  $p < 0.01$ ) (Table 2). Significant differences were observed between patients who had clinically severe trauma and AIS scores  $\geq 2$  and those with no severe trauma and AIS scores  $< 2$  in terms of WBC, Neu, MPV/W, and WBC/N (Table 3).

A negative correlation was detected between the AIS score and MPV/W ( $r = -0.282$ ;  $p < 0.05$ ) and MPV/N ( $r =$

**Table 1.** The clinical characteristics of the patients

Patients n (%)	
Age (median, IOR)	3 (1-7)
Sex (male/female)	59/27 (68.6/31.4)
<b>Symptoms/signs</b>	
Vomiting	
< 3	13 (15.1)
$\geq 3$	9 (10.5)
headache	7 (8.1)
Loss of consciousness > 5 sn	7 (8.1)
seizure	1 (1.2)
Frontal hematoma	12 (13.9)
Occipital hematoma	10 (11.6)
Parietal/temporal hematoma	19 (22)
<b>Clinically severe trauma +</b>	13 (15.1)
<b>Mechanism of injury</b>	
fall from height	26 (30.2)
low energy injury	49 (56.9)
in car- accident	8 (9.3)
out-car accident	2 (2.3)
bike/motorcycle injury	1 (1.1)
<b>Head CT +/ head CT-</b>	36 /50
Isolated linear / depressed fracture	18/2
linear fracture + IC hemorrhage	6
IC hemorrhage + depressed fracture	1
Linear fracture + contusion	3
IC hemorrhage without skull fracture	13
AIS score $\geq 2$ / $< 2$	14/72 (16.3/83.7)
discharge from pediatric emergency room	60 (69.7)
admission to the wards	18 (20.9)
admission to PICU	3 (3.4)
underwent operation	5 (5.8)

**Table 2.** Comparison of CBC markers in the study groups and control group

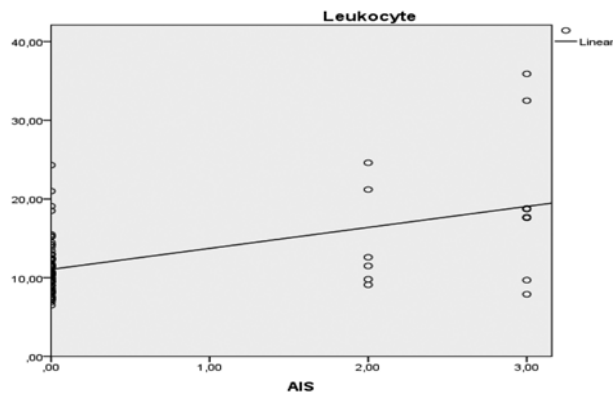
	Study group (min-max)		Control group (min-max)	p
Age (years)	3 (1-7)		6 (1-7)	,439
Sex (n) (female/male)	27/59		69/186	
	<b>CT +</b>	<b>CT -</b>		
WBC (/I)	<b>12.2</b> (9.7-18.7)	<b>10.4</b> (8.5- 12,4)	<b>8,5</b> ( 7.1-10,9)	<b>&lt; 0,001</b> <sup>a,b,c</sup>
Neu (/I)	<b>7.1</b> (4.4-14.6)	<b>4,7</b> (2.9-6,3)	<b>3.3</b> (2.5-4.4.7)	<b>&lt; 0,001</b> <sup>a,b,c</sup>
Plt ( $\times 10^{-3}$ )	293 (237-393)	312.5 (257.5- 383.7)	290 (233.2-233.2)	0,440
PDW	16.4 (16.3-16.7)	16.4 (16,1-16.7)	16.5 (16.1-17)	0,607
Pct	,25 (,20-,29)	,24 (,20-,29)	,24 (,20-,29)	0,855
MPV (fl)	<b>7.7</b> (7.3-8.6)	<b>7.6</b> (7.2-8.1)	<b>8.4</b> (8.1-9.)	<b>&lt; 0,001</b> <sup>a,b,c</sup>
MPV/WBC	<b>,64</b> (,42-,85)	<b>,74</b> (,62-,86)	<b>1</b> (,78-1,2)	<b>&lt; 0,001</b> <sup>a,b,c</sup>
MPV/Neu	<b>1,16</b> (,57-1,6)	<b>1,5</b> (1,2-2,6)	<b>2,5</b> (1,8-3,4)	<b>&lt; 0,001</b> <sup>a,b,c</sup>
MPV/Pl	<b>,026</b> (,018-,035)	<b>024</b> (,019-,029)	<b>,029</b> (,024-,037)	<b>&lt; 0,001</b> <sup>a,b</sup>

a: CT+ vs control; b: CT- vs control; c: CT + vs CT -

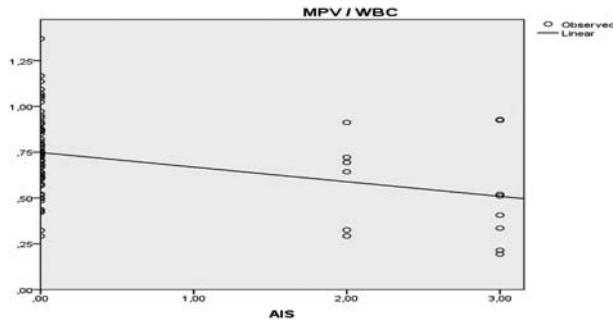
**Table 3.** Comparison of CBC markers regarding to trauma severity and AIS score

	Sever trauma + (min-max)	Sever trauma - (min-max)	p	AIS < 2	AIS ≥ 2	p
WBC (/l)	13.9 (10.7-22.9)	10.5 (8.60-12.4)	.020	9.8 (8.3-12.9)	18.2 (10.4-23.7)	.007
Neu (/l)	9.9 (6.4-16)	4.7 (3.2-6.9)	< 0.001	4.8 (3.1-7.5)	14.7 (6.1-16.9)	.002
Plt (x10 <sup>-3</sup> )	354 (290-388)	303 (246-383)	.193			
Pct	.27 (.24-.29)	.23 (.20-.28)	.069	.23 (.20-.28)	.25 (.17-.27)	NS
PDW	16.4 (16.3-16.5)	16.4 (16.2-16.8)	.840			
MPV (fl)	8 (7.05 -8.40)	7.6 (7.20-8.20)	.592	7.80 (7.50-8.45)	7.65 (6.97-6.97)	NS
MPV/W	.57 (.30-.78)	.73 (.61-.87)	.020	.78 (.62-.91)	.45 (.30-.77)	.016
MPV/N	.81 (.42-1.28)	1.52 (1.11-2.31)	< 0.001	1.51 (1.10-2.60)	.56 (.42-1.27)	.005

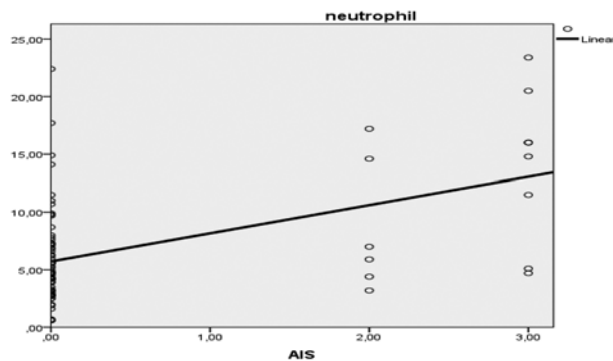
-0.335; p < 0.05) (Figure 1b, 1 d). By contrast, a positive correlation was observed between the AIS score and WBC (r = 0.316; p < 0.05) and the AIS score and Neu (r



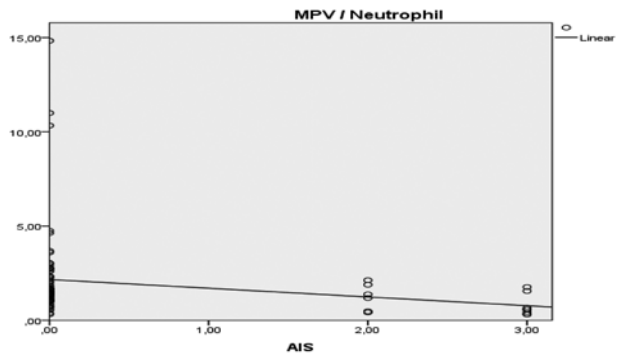
**Figure 1a:** Correlation graph between WBC and AIS score



**Figure 1b:** Correlation graph between MPV/W and AIS score

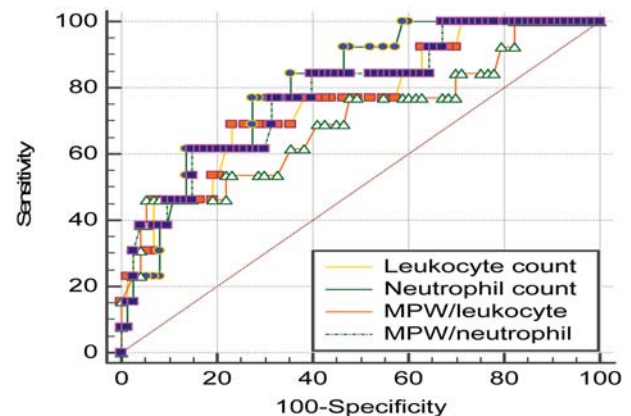


**Figure 1c:** Correlation graph between Neutrophil and AIS score (p < 0.05, r = ,365)



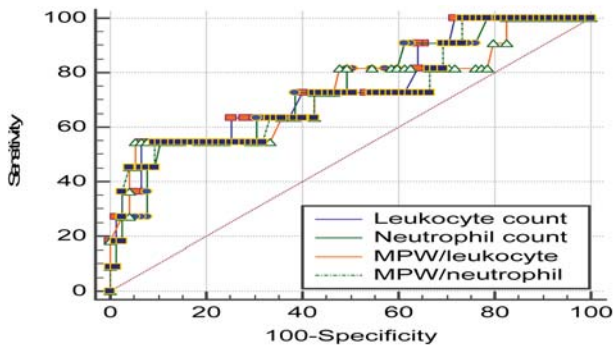
**Figure 1d:** Correlation graph between MPV/N and AIS score

= 0.365; p < 0.05) (Figure 1a, 1c). Neu and MPV/N exhibited under the curve (AUC) values of 0.805 (95% confidence interval [CI], 0.70–0.88; p] and 0.782 (95% CI, 0.68–0.86; p) respectively for differentiating patients with MHT and severe trauma from those with no severe trauma (Figure 2a). Setting the WBC cut-off value to > 18.5 and the MPV/W cut-off value to ≤ 0.41 gave 99.33% and 94.67% specificity, respectively, for differentiating MHT patients with AIS scores > 1 from



Variable	AUC	SE <sup>a</sup>	95% CI <sup>b</sup>	Cut-off	sensitivity	specifity
WBC	0,761	0,0753	0,657 to 0,847	>12.5	69.23	76.21
Neu	<b>0,805</b>	0,0585	0,706 to 0,883	>6.9	76.92	72.60
MPW/W	0,701	0,0902	0,592 to 0,795	≤0.41	46.15	94.52
MPW/N	0,782	0,0701	0,680 to 0,864	≤0.9	61.54	84.93

**Figure 2a:** The ROC curves of variables for the presence of severe trauma



Variable	AUC	SE	95% CI	Cut-off	sensitivity	specificity
WBC	0,746	0,0899	0,641 to 0,834	>18,8	54,55	93,33
Neu	0,739	0,0857	0,634 to 0,828	>11	54,55	89,33
MPW/W	0,726	0,0989	0,619 to 0,817	≤0,41	54,55	94,67
MPW/N	0,724	0,0948	0,617 to 0,815	≤0,66	54,55	90,67

**Figure 2b:** The ROC curves of variables for AIS > 1

those with AIS scores < 1 (Figure 2b). When differentiating the patients who had clinically severe trauma from patients who do not, setting the MPV/W cut-off value to  $\leq 0.41$  gave a specificity of 94.52% (Figure 2a).

## DISCUSSION

This study demonstrated that WBC and Neu levels in children with MHT were significantly higher than those in healthy controls. Furthermore, a progressive increase in WBC and Neu levels occurred in parallel with the presence of head CT pathologies. The elevated levels of WBC, particularly Neu in children with MHT, indicated a post-traumatic inflammatory response (11, 14, 15, 16). It was clear from our sample that WBC and Neu levels were significantly higher in the head CT-negative MHT group than the healthy controls. This result suggests that the stress of trauma itself can result in marked demargination of leukocytes even in patients who do not sustain a significant injury. Furthermore, in the current study, WBC and Neu levels were positively correlated with trauma severity and the AIS score. Rovlias *et al.* reported that patients with a severe head injury have significantly higher WBC counts than those with moderate or MHT (14). In fact increased cortisol and catecholamine are responsible for the increase in the WBC count in patients with head trauma and patients with a higher WBC count on admission often have a poorer outcome (14, 17, 18). Our study provides evidence for the involvement of WBC and Neu after MHT. In particular, Neu counts could provide additional information about trauma severity and the presence of brain pathologies on head CT scans in children with MHT. Nevertheless, the increased WBC and Neu counts alone in parallel with the presence of brain injury and clinically severe trauma may reflect the stress response.

Could PVI alone or in combination with WBC count be of diagnostic value for brain injury after MHT? MPV and PDW represent platelet size and are potential

biomarkers of platelet activity. However, only MPV values appeared to be of significance in patients with MHT in our study. This finding is compatible with the literature that among all variables produced by complete blood count analyses, MPV is better and well-standardized than PDW (19, 20). An increase in the MPV value suggests an increased release of a larger number of hyperactive platelets from the spleen, whereas a decrease in the MPV value may be due to consumption of larger platelets which occurs in sepsis, high-grade systemic inflammatory diseases, and an acute attack of familial Mediterranean fever in children (21, 22, 23). MPV values increase in some clinical situations such as cardiovascular disorders, stroke, and cancers (8-10, 24). The most important result of the current study was that within 24 h of injury MPV values decreased compared to healthy controls although there was no pathology on a head CT scan. Unlike the results of previous studies on head trauma, the decrease in MPV values was unexpected (11, 12). However, a similar finding was reported in a study of 54 adult patients with MHT (13). The results of that study also demonstrated that a progressive decrease in MPV occurs in parallel with the severity of MHT (13). A possible explanation could be the consumption of larger platelets at the site of leukocyte migration immediately after the trauma. An inverse relationship has been reported between platelet count and MPV under physiological and some pathological conditions to maintain haemostasis by preserving a constant platelet mass (25). We did not find any significant difference in the platelet count between the study and control groups. Although we cannot explain the pathology underlying the significant decrease in MPV with a normal platelet count, we believe that MHT without a brain injury would have a different effect on platelet biology, as physical damage may result in a higher prevalence of hypo reactive platelets than that in patients in other clinical situations (8-10, 24, 26). Our results also did not show any differences in MPV levels regarding trauma severity or the AIS score. However, if we investigated serial MPV measures in our study, we would have a better idea about the balance between selective consumption of larger platelets and the ability of the bone marrow to replace platelets in patients with acute isolated MHT.

When we examined the ratio of parameters that increased and decreased within 24 h after MHT, the results showed that the MPV/W, MPV/N, MPV/PL ratios of the study groups significantly decreased compared to the healthy blood donors. Moreover, the MPV/W and MPV/N ratios were significantly lower in patients with head CT pathologies than in those with a normal head CT scan.

The results of our study have some clinical implications. This study provides evidence for the involvement of WBC, Neu, and MPV within 24 h following

MHT. Although many markers have been studied and defined, CBC is easily accessible and inexpensive to perform in clinical practice. The MPV/W and MPV/N ratios provided additional information about trauma severity in children with isolated MHT and may be useful for patients with MHT who are being observed for possible traumatic brain injury.

Some limitations of our study should be mentioned. The study sample was small, and we did not conduct a serial CBC count for the patients. If serial CBCs were assessed, then possible changes in MPV and platelet count and the balance between thrombopoiesis and inflammation in patients with severe trauma after MHT would have been clearly revealed.

We suggest that the diagnostic performance of the MPV/N ratio for identifying clinically severe trauma in children with MHT (i.e., AUC of 0.78;  $p = 0.01$ ) with sensitivity and specificity of 0.61 and 0.84, respectively for values  $< 0.9$  provides a reliable basis for planning further investigations.

## CONCLUSION

The MPV/W and MPV/N ratios can be used as markers for the severity of injury in patients with MHT presenting to the paediatric emergency room when the necessity for a head CT scan is unclear.

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Emel Atas Berksoy and Murat Anil were involved in the conception and design of the study, and analysis and interpretation of data. Murat Anil and Emel Atas Berksoy drafted the article or revised it critically for important intellectual content. All authors approved the final

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## Availability of data and materials

The authors declare that no data have been fabricated or manipulated (including images) to support your conclusions. The authors declare that no data, text, or theories by others are presented as if they were the authors own.

## Informed consent

Written informed consent was not necessary because no patient data has been included in the manuscript.

## Human rights

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Ethical approval

We confirm that Ethical Committee approval was sought where necessary and is acknowledged within the text of the submitted manuscript.

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## Sažetak

# EFIKASNOST PARAMETARA KOMPLETNE KRVNE SLIKE ZA PREDVIĐANJE INTRAKRANIJALNE POVREDE KOD DECE SA MANJIM TRAUMAMA GLAVE

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**Cilj:** Cilj nam je bio da istražimo odnos između težine traume i broja trombocita (PI) i leukocita (WBC) za identifikaciju traumatske povrede mozga (TBI) kod dece sa manjim traumama glave (MHT).

**Materijal i metode:** Ova prospektivna studija obuhvatila je decu sa akutnim traumama glave koja su podvrgnuta kompjuterskoj tomografiji glave (CT) na osnovu kriterijuma Pedijatrijske istraživačke mreže hit-

ne pomoći (PECARN). Evaluirane su vrednosti srednjeg volumena trombocita (MPV), širina raspodele trombocita (PDW), odnos srednjeg volumena trombocita i trombocita (MPV/PL), odnos srednjeg volumena trombocita i leukocita (MPV/WBC), kao i odnos srednjeg volumena trombocita i neutrofila (MPV/Neu).

**Rezultat:** 86 dece sa MHT i 245 kontrola su uključeni u studiju. WBC, broj neutrofila, MPV, MPV/WBC, MPV/Neu kao i MPV/PI razmere bile su statistički drugačije kod pacijenata sa abnormalnim tomografijama glave,

kod pacijenata sa normalnom tomografijama i u kontrolnoj grupi ( $p < 0.05$ ). Za predviđanje skraćene ocene povrede (AIS)  $> 1$ , AUC vrednosti WBC-a, neutrofila, MPV/WBC i MPV/Neu bile su 0.746, 0.739, 0.726 i 0.724.

**Zaključak:** Kod dece sa MHT koja su podvrgnuta CT snimanju, WBC, Neu, MPV/WBC i MPV/Neu mogu biti korisni za predviđanje ozbiljnosti traume u pedijatrijskom odeljenju hitne službe.

**Ključne reči:** deca, kompletna krvna slika, povrede glave, intrakranijalna povreda.

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