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Mean platelet volume dynamics as a prognostic indicator in pediatric surgical intensive care unit: a descriptive observational study

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Abstract

Background: Platelet size and activity have a close correlation. The mean platelet volume (MPV) is related to the disease severity and prognosis, especially in critically ill patients.

Objective: To study the relation between MPV changes and postoperative morbidities and mortality in pediatric surgical intensive care unit (PSICU).

Methods and material: We enrolled in this descriptive observational study one hundred PSICU children aged from 1 month to 18 years and stayed for > 48 h for peri-operative or post-trauma management. The 1ry outcome was the association between percentage change in MPV (Δ MPV) value and mortality. We recorded MPV, Δ MPV, and platelet count as a baseline, at day 0, 1st, 2nd, 3rd, 5th, and 7th days and then once weekly until patients were discharged, died, or reached a maximum of 90 days in ICU stay.

Statistical analysis used: We used statistical package for the social science (SPSS) version 22. Non-parametric Mann-Whitney test made comparisons between quantitative variables. Repeated measures analysis of variance (ANOVA), non-parametric Friedman, and Wilcoxon signed-rank tests made the comparison within the same patients. We used receiver operating characteristic (ROC) curves for the detection of sensitivity and specificity.

Results: Patients who developed ICU complications showed higher Δ MPV compared with non-complicated cases, and this was statistically significant on days 2, 3, 5, and 7 of ICU stay. ROC curve analysis showed a sensitivity of 57.2% and 73% on days 2 and 3 and a specificity of 76.6% and 71% on days 2 and 3, respectively.

Conclusions: MPV dynamics have a prognostic role and worth a value in predicting several complications in PSICU.

Keywords: Platelet, Mean platelet volume, Pediatric, Surgical intensive care unit, Prognosis

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Key messages

Mean platelet volume (MPV) dynamics worth a value in predicting several complications in critically ill pediatric surgical patients.

However, platelet count seemed to be a more specific and sensitive tool to detect complications than MPV dynamics.

Background

Platelets have a major role in hematopoiesis, fibrin deposition, and inflammation (Archana, Vijaya, & Jayalakshmi, 2014). The platelet count is dynamic (Greinacher & Selleng, 2010). In critically ill patients, platelet consumption is frequent and associated with a poorer prognosis (Zampieri et al., 2014). As platelet size correlates to activity, the mean platelet volume (MPV) is a reflection of its size, function, and activation (Karadag-Oncel et al., 2013; Sezgi et al., 2014; Slavka et al., 2011). MPV seems to be a marker of platelet production, consumption, and disease severity (Archana et al., 2014). So, changes in MPV could be used for disease prognosis and mortality in ICU (Sezgi et al., 2014). We hypothesized that MPV changes could be used as a prognostic tool in the pediatric surgical intensive care unit.

Methods

We conducted this descriptive observational study on one hundred pediatric surgical patients who were admitted to pediatric surgical intensive care units (ICUs) at University Hospitals started from January 6, 2015, to January 12, 2015. This study aimed to assess the prognostic value of mean platelet volume (MPV) dynamics in the pediatric surgical intensive care unit.

After approval by the departmental Research Ethics Committee; we obtained informed consents from parents or the next-of-kin of patients before commencement, and 100 pediatric cases aged from 1 month to 18 years who admitted to pediatric surgical ICUs and stayed for > 48 h for perioperative or post-trauma management were enrolled in the study. We excluded from the study children who stayed for < 48 h in the ICU and those who had congenital heart disease, hematological disorder, or with a current diagnosis of cancer.

We calculated the sample size according to this equation:

Sample size =

$$\text{Sample size} = \frac{Z_{1-\alpha/2}^2 SD}{d^2}$$

Where,

$Z_{1-\alpha/2}$ = is standard normal variate (at $p < 0.05$, it is 1.96)

SD = standard deviation of the variable. Value of standard deviation was taken from a previous study, which was 5 [4]

d = absolute error or precision which is 1

Power of study which is the chance of a study successfully demonstrating the “true” result is 80%

Alpha (α) error which is the probability of falsely rejecting a true null hypothesis is 5%

Beta (β) error, which is the probability of failing to reject a false null hypothesis, is 20%.

We used the G*Power version 3.1.9.2, program written by Franz Faul, Universitat Kiel, Germany, Copyright (C): 1992–2014 for sample size calculation.

After patient admission to ICU, we collected the following data: age in months, gender, weight in kilogram, the name of ICU to which the patient admitted, primary reason for admission, and source of referral (either from the operating room (OR), emergency room, or inpatient ward). Also, we recorded the duration of surgery in surgical patients, the need for intra-operative blood or platelets transfusion, and the number of units transfused as an indicator of significant blood loss. We recorded intra-operative complications including hypotension (defined as a reduction $\geq 20\%$ in systolic blood pressure (SBP) from baseline reading), significant blood loss, desaturation (defined as oxygen saturation < 95% for more than 10 s), and arrhythmias. Moreover, we recorded the length of stay (LOS) in the ICU and the fate of the patient afterward (discharge or death).

The following laboratory data were obtained and recorded: mean platelet volume (MPV) in femtoliter (fl) and platelet count (PLC) in 10^3 per microliter ($10^3/\mu\text{L}$). The attending intensivist obtained a blood sample of 2 ml of blood by either venipuncture, arterial puncture, or through a central catheter if it was in situ to get accurate complete blood count (CBC) results. Then, samples collected in ethylene diamine tetra-acetic acid (EDTA) containing tubes and analyzed in the hematology laboratory of the hospital in an automated hematology analysis system (Sysmex NE 8000 autoanalyzer, Sysmex Europe GmbH, Norderstedt, Germany) that measures platelet size using aperture-impedance technology. All patient samples were processed within an hour after collection, as recommended in the literature, to avoid bias due to excessive platelet swelling. The normally accepted values for MPV at our “University Hospitals’ hematology laboratory” ranged from 7 to 11 fl. All laboratory parameters were recorded as a baseline (pre-operative values), at the day of ICU admission (day 0), 1st, 2nd, 3rd, 5th, and 7th days and then once weekly until patients were discharged, died, or reached the greatest of 90 days in ICU stay. To measure the daily MPV changes, we constructed and computed ΔMPV . We defined ΔMPV as: $\Delta\text{MPV} = ([\text{MPV day}(X) - \text{MPV day}(0)]/\text{MPV day}(0) \times$

100% where MPV day(X) was the MPV value for day(X) in ICU while MPV day (0) was the MPV value for that collected at ICU admission (day 0). Δ MPV recorded at days 1 (24 h after ICU admission), 2, 3, 5, and 7, then once weekly until patients had been discharged, died, or reached the greatest of 90 days in ICU stay. Pediatric Index of Mortality (PIM) score was calculated from data collected on admission day (day 0) to ICU and computed electronically from the following website: SFAR Société Française d'Anesthésie et de Réanimation (<http://www.sfar.org/scores2/pim2.html#underlying>) for prediction of mortality. We also calculated the Pediatric Logistic Organ Dysfunction (PELOD) Score for each child daily.

The 1ry outcome of this study was the association between percentage change in MPV (Δ MPV) value and patient mortality in pediatric surgical patients admitted to pediatric surgical ICUs at University Hospital between January 6, 2015, and January 12, 2015.

Secondary outcomes included as follows:

- The association between percentage change in MPV (Δ MPV) value starting from the day of ICU admission and postoperative morbidities that were recorded in PSICU and included fever, surgical bleeding, sepsis, pneumonia, the need of mechanical ventilation, the use of vasopressor agents, and the necessity of blood or platelet transfusion. We defined fever as a core body temperature $> 38^{\circ}\text{C}$, while the intensivist made the diagnosis of sepsis and pneumonia according to ICU definitions. Surgical bleeding is described as a bleeding episode resulting in drop-in hemoglobin of > 2 g/dl within 24 h, bleeding events requiring local tamponade or blood transfusion within 24 h.
- And the association between platelets count (PLC) starting from the day of ICU admission and postoperative morbidities and mortality.

Statistical methods

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 22. Data were summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were made using the non-parametric Mann-Whitney test. Probability (p) values less than 0.05 were considered statistically significant, and p value < 0.001 was considered highly significant. Repeated measures (ANOVA), non-parametric Friedman, and Wilcoxon signed-rank tests made the comparison of serial measurements

within the same patients for quantitative variables. We used receiver operating characteristic (ROC) curves for the detection of sensitivity and specificity of different parameters.

Results

In this descriptive observational study, we have enrolled one hundred patients who fulfilled the inclusion criteria. Tables 1 and 2 show patients' characteristics and demographic data, while Table 3 shows reported intraoperative complications.

Platelet count (PLC) showed a gradual decrease in number over the first few days in ICU compared to admission day (Fig. 1); then, it started to increase from day 7. Although the changes in platelet count (PLC) during the 1st week of ICU stay were within a normal range, these changes showed a significant difference (p value = 0.00) compared to the preoperative platelet count for surgical cases. Also, these changes showed a significant difference (p value = 0.00) compared to day 0 except for day 7, the p value was 0.623.

Consequently, mean platelet volume (MPV) showed a gradual increase in the amount over the first few days in ICU compared to admission day (Fig. 2); then, it started to decrease again. Although the changes of MPV during the 1st week of ICU stay were within a normal range, these changes showed a significant difference (p value = 0.00) compared to the preoperative MPV value in surgical cases except for day 7 in which p value = 0.077. Also, these changes of MPV at different days showed a significant difference (p value = 0.00) compared to day 0 MPV value.

Percentage changes in MPV (Delta Δ MPV) increased in day 2 and day 3 in comparison to day 1 changes, then

Table 1 Patients' demographic data. Data presented as mean \pm standard deviation (SD), count, and frequency

Variable	Mean (\pm SD) ^a /count (frequency)		
Age (months)	50.82 \pm 38.84		
Weight (kg)^b	15.83 \pm 8.06		
Gender			
Male	55 (55.0%)		
Female	45 (45.0%)		
Duration of surgery (h)	1.69 \pm 0.99		
Variable	Median	Minimum	Maximum
PELOD^c Score (admission)	0.00	0.00	41.00
PIM Score^d	0.80	0.20	15.40

^aSD, standard deviation

^bkg, kilogram

^cPELOD, Pediatric Logistic Organ Dysfunction Score

^dPIM, Pediatric Index of Mortality score

Table 2 Patients' characteristic. Data presented as mean \pm standard deviation (SD), count, and frequency

Variable	Mean (\pm SD ^a)/count (frequency)
Length of ICU^b stay (days)	6.14 \pm 3.25
Day of ICU discharge	5.16 \pm 3.26
Cases transferred from	
Operative room	72 (72.0%)
Emergency room	16 (16.0%)
Inpatient ward	12 (12.0%)
Type of cases	
Preoperative	5 (5.0%)
Trauma	22 (22.0%)
Evacuation of extradural hematoma	4 (4.0%)
Exploration for intestinal obstruction	42 (42.0%)
Splenectomy	5 (5.0%)
Exploration for strangulated hernia	6 (6.0%)
Fundoplication for diaphragmatic hernia	6 (6.0%)
Closure of ileostomy	4 (4.0%)
Myotomy for congenital hypertrophic pyloric stenosis	6 (6.0%)
Try indication for ICU admission in postoperative cases	
Disturbed conscious level (DCL)	12 (12.0%)
Postoperative monitoring	58 (58.0%)
Sepsis	10 (10.0%)
Respiratory distress	7 (7.0%)
Massive blood transfusion	5 (5.0%)
Desaturation at room air	8 (8.0%)

^aSD, standard deviation^bICU, intensive care unit

decreased again in day 5 and day 7. Percentage changes in MPV (Delta Δ MPV) at different days of the first week of ICU stay showed a significant difference compared to day 1 Δ MPV value, as shown in Fig. 3.

Among the studied one hundred patients, fifty-four patients (54%) had complications that developed during their ICU stay. These complications varied from sepsis, pneumonia, fever, use of vasopressor agents, and need to mechanical ventilation to the need for blood or platelets transfusion (Fig. 4).

PLC among ICU complicated versus non-complicated patients during the first week of ICU stay presented in Fig. 5. Patients who developed ICU complications showed lower PLC compared to non-complicated cases. This association was statistically significant on days 1, 2, and 3 of ICU stay, but it is insignificant on days 5 (p value = 0.861) and 7 (p value = 0.247).

When comparing PLC among ICU complicated versus non-complicated cases at day 1 by ROC curve analysis, there was a significant difference of platelets count

Table 3 Intraoperative complications. Data presented as mean \pm standard deviation (SD), count, and frequency

Variable	Mean (\pm SD ^a)/count (frequency)
Intraoperative complications	
No complications	66 (66.0%)
Hypotension with significant blood loss	25 (25.0%)
Significant blood loss with no hypotension	6 (6.0%)
Desaturation	3 (3.0%)
Need for intra-operative blood or platelets transfusion	
Yes	42 (42.0%)
No	58 (58.0%)
Units of transfused blood	
No	58 (58.0%)
1st dose of PRBCs (= 10 ml/kg)	37 (37.0%)
2nd dose of PRBCs (= 5 ml/kg)	5 (5.0%)

^aSD, standard deviation

between complicated cases and non-complicated cases ($p < 0.001$; area under the curve = 0.789; 95% confidence interval = 0.688–0.890). According to ROC curve analysis, the sensitivity of platelet counts to detect complications at day 1 was 81.4%, but the specificity of platelet counts to detect complications at day 1 was 71.9%. ROC curve analysis at day 2 proved a significant difference of PLC between complicated cases and non-complicated cases (p value < 0.001 ; area under the curve = 0.889; 95% confidence interval = 0.812–0.965). The sensitivity of PLC to detect complications at day 2 was 81.1%, but the specificity of PLC to detect complications at day 2 was 100%.

Patients who developed ICU complications showed a higher Delta MPV compared to non-complicated cases. This association was statistically significant on days 2, 3, 5, and 7 of ICU stay, but it is insignificant on day 1 (Fig. 6).

When comparing Delta MPV between ICU complicated and non-complicated cases at day 1 by ROC curve analysis, there was an insignificant difference of Delta MPV between complicated cases and non-complicated cases ($p = 0.691$; area under the curve = 0.523; 95% confidence interval = 0.409–0.637). ROC curve analysis of Delta MPV at day 2 showed a significant difference of Delta MPV between complicated cases and non-complicated cases ($p = 0.035$; area under the curve = 0.623; 95% confidence interval = 0.514–0.732). The sensitivity of Delta MPV to detect complications at day 2 was 57.2%, but the specificity of it to recognize complications at day 2 was 76.6% (Fig. 7).

ROC curve analysis of Delta MPV at day 3 demonstrated a significant difference of Delta MPV between complicated cases and non-complicated cases ($p < 0.001$;

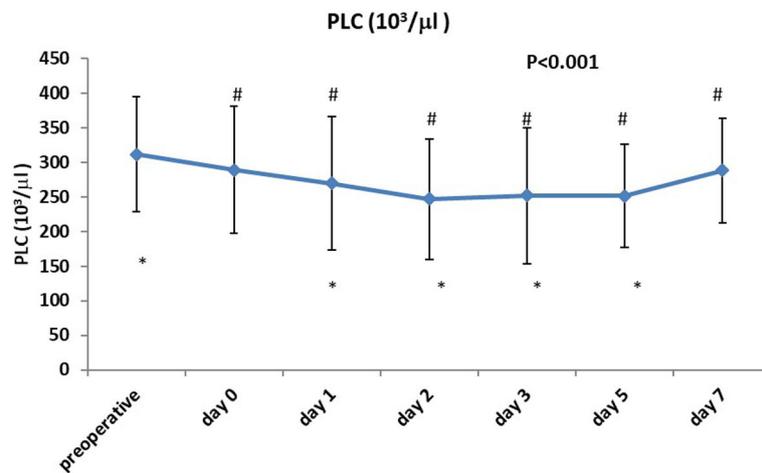


Fig. 1 PLC changes during 1st week of ICU stay. Data presented as means; error bars represent standard deviation. $p < 0.001$ = highly significant. The number sign (#) indicates highly significant difference compared to preoperative PLC. The asterisk (*) indicates highly significant difference compared to day 0 PLC

area under the curve = 0.794; 95% confidence interval = 0.700–0.888). According to ROC curve analysis, the sensitivity of Delta MPV to detect complications at day 3 was 73%, while the specificity of it to detect complications at day 3 was 71%. ROC curve analysis of Delta MPV (Fig. 8) of the day 5 showed a significant difference of Delta MPV between complicated cases and non-complicated cases ($p < 0.001$; area under the curve = 0.810; 95% confidence interval = 0.697–0.922). The sensitivity of Delta MPV to detect complications at day 5 was 100%, but the specificity of Delta MPV to recognize complications at day 5 was 76.2%.

ROC curve analysis of Delta MPV at day 7 revealed a significant difference of Delta MPV between complicated cases and non-complicated cases ($p = 0.018$; area under the curve = 1.000; 95% confidence interval = 1.000–

1.000). According to ROC curve analysis, the sensitivity of Delta MPV to detect complications at day 7 was 100%, and the specificity of Delta MPV to detect complications at day 7 was 100%.

In this study, there was only one reported case of mortality. That mortality case associated with a daily reduction of platelet counts compared to the remaining non-mortality cases. Although of this finding, this difference was statistically insignificant because of the presence of only one case of mortality within the one hundred cases and thus making the comparison very difficult. This mortality case was a 5-year-old child who admitted to the hospital after a road traffic accident with Glasgow Coma Scale three and a large extradural hematoma. He underwent evacuation of that hematoma and was admitted after that to ICU for mechanical ventilation and

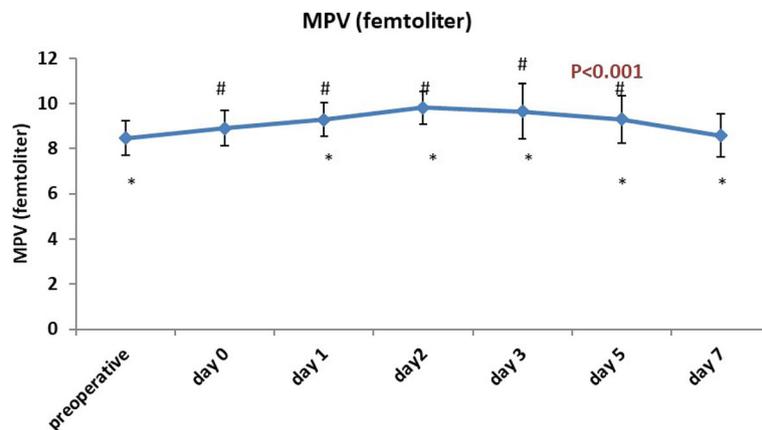
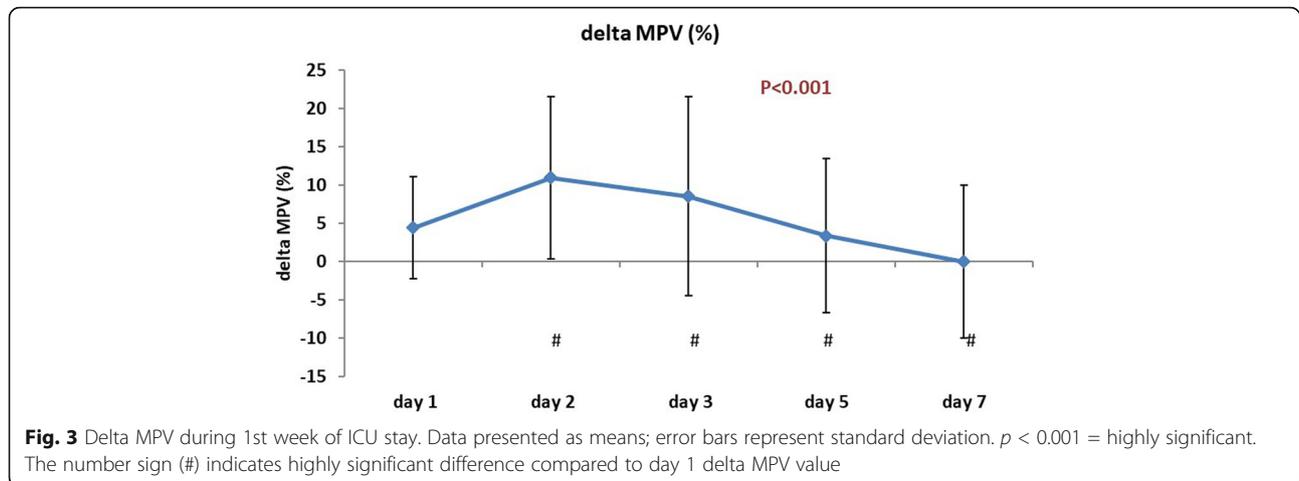


Fig. 2 MPV changes during 1st week of ICU stay. Data presented as means; error bars represent standard deviation. $p < 0.001$ = highly significant. The number sign (#) indicates highly significant difference compared to preoperative MPV. The asterisk (*) indicates highly significant difference compared to day 0 MPV



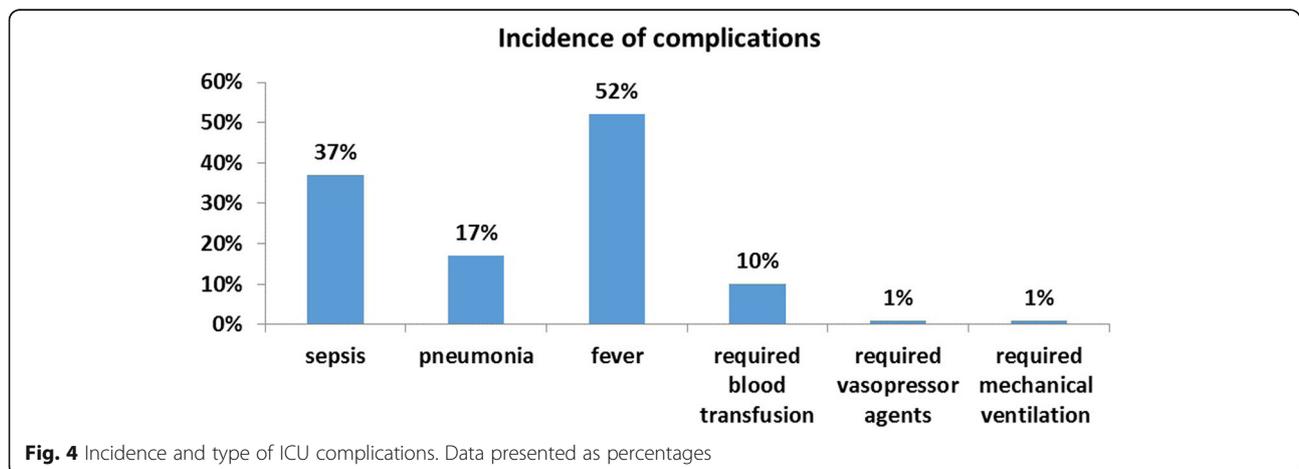
vasopressor drug support. This patient died on the 3rd postoperative day. We found that the percentage change in MPV increased daily in the mortality case compared with the remaining non-mortality cases. That finding was also statistically insignificant (p value = 0.086). This insignificance may be explained by the presence of only one mortality case within the 100 cases, thus making the comparison very difficult.

Discussion

Mean platelet volume (MPV) is a reflection of platelet size and, consequently, platelet function and activation (Machlus & Italiano, 2013; Yuri Gasparyan, Ayvazyan, P Mikhailidis, & D Kitas, 2011). MPV is an essential, simple, readily available, and cost-effective tool (Van der Lelie & Von dem Borne, 1983). Platelet count has an inverse relationship with MPV (Kim et al., 2015).

Although we failed to find a significant correlation between MPV and mortality, the current study suggests that trends in changes in MPV may be more reliable markers of poor prognosis than the corresponding absolute values. To the best of our knowledge, it is the first time to study the relationship between change in MPV and mortality and morbidities that occurred at pediatric surgical ICU.

Several studies assessed MPV in critical illness. Zampieri et al. (2014) found an increase in MPV in the first 24 h after admission independently associated with increased mortality. Van der Lelie and Von dem Borne (1983) showed a higher MPV in patients with sepsis than in patients with localized infection and suggested that an increase of MPV in patients with bacterial infection could indicate the occurrence of septicemia. Kim et al. (2015) noted that continuous measurement of MPV could be useful in determining mortality risk in patients



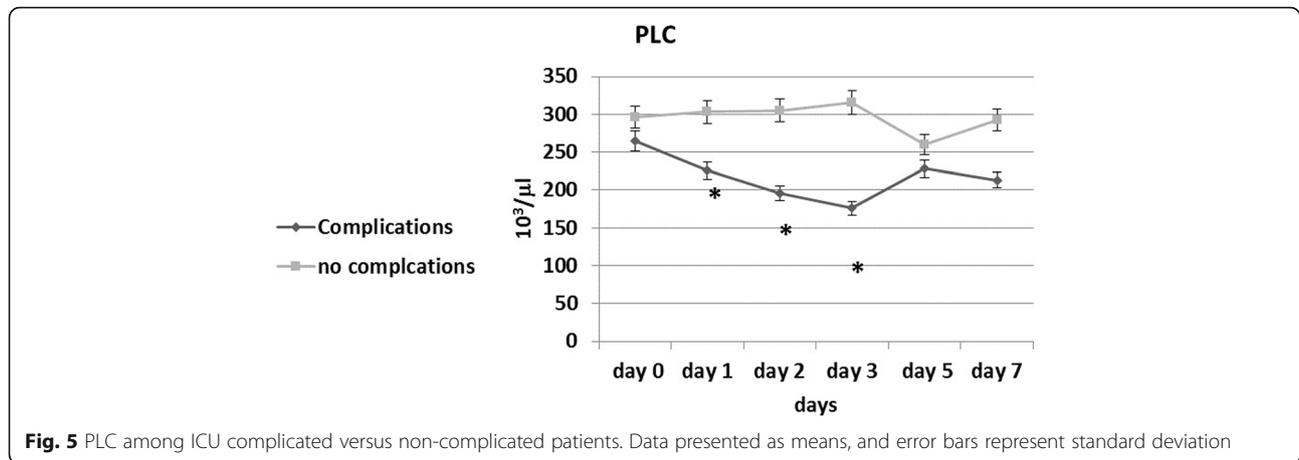


Fig. 5 PLC among ICU complicated versus non-complicated patients. Data presented as means, and error bars represent standard deviation

with sepsis and septic shock. Guclu, Durmaz, and David (2013) reported low platelet counts and higher MPV in patients with severe sepsis compared with other control patients. Aydemir, Piskin, Akduman, Kokturk, and Aktas (2012) said that fungal sepsis has a stronger association with thrombocytopenia and increased MPV. Unal, Ozen, Kocabeyoglu, et al. (2013) stated a clear association of preoperative MPV and hematocrit levels with post-coronary artery bypass grafting (CABG) adverse events. The prognostic value of these measures was independent of other well-defined individual risk factors. In contrast, white blood cell (WBC) count, including differential leukocyte count, failed to demonstrate a significant relationship with post-CABG adverse events. In an extensive prospective study, Oncel et al. (2012) also reported high MPVs in septic newborns. This study was the first one to demonstrate a statistically significant difference concerning baseline MPV values (day 0 value) between neonates with sepsis (proven or clinical) and healthy

controls. Rowe, Buckner, and Newmark (1975) examined 93 postoperative pediatric surgical patients and found that 71% of the patients with Gram-negative sepsis had platelet counts $\leq 100,000$, whereas all the platelet counts in the non-septic or Gram-positive sepsis patients were $\geq 150,000$. They also noted a rise in platelet counts when patients efficiently treated for sepsis. Also, Rastogi, Olmez, Bhutada, and Rastogi (2011) demonstrated a significant association of mortality and significant morbidities in preterm newborns below 28 weeks gestations, and platelets drop in the first 7 days of life. Agrawal and Sachdev (2008) stated that thrombocytopenic children have a higher incidence of bleeding, longer ICU stay, and higher mortality.

These results are consistent with the current study findings, and together, these data suggest that continuous monitoring of changes in MPV and platelet counts may play a role in risk stratification of patients with morbidities and mortality in pediatric surgical ICU.

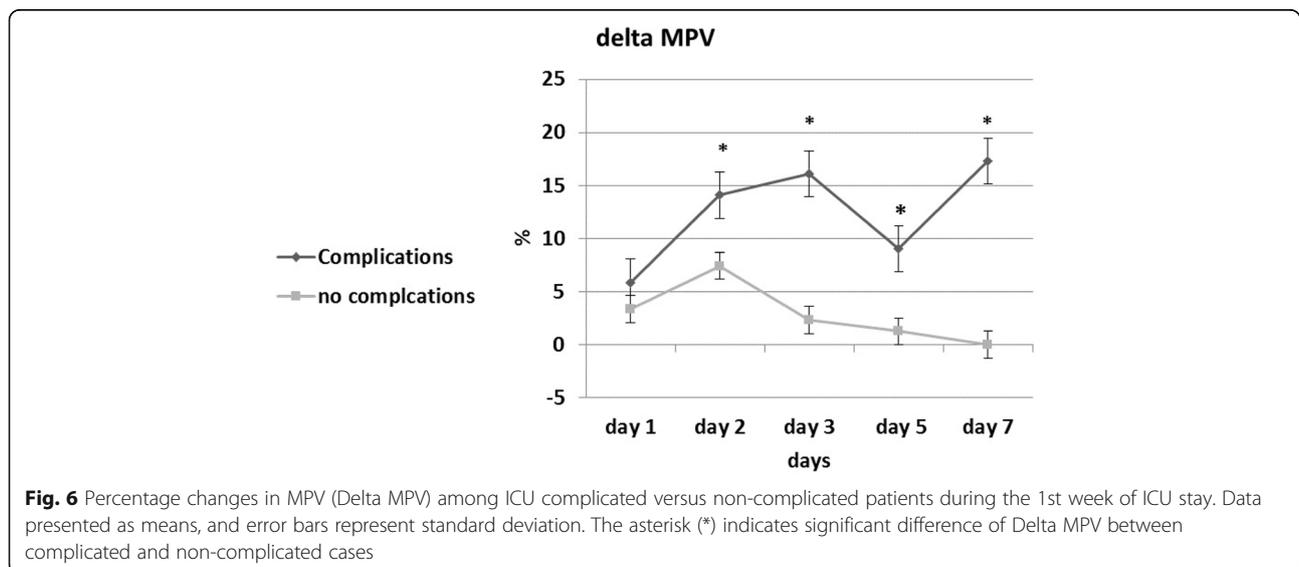
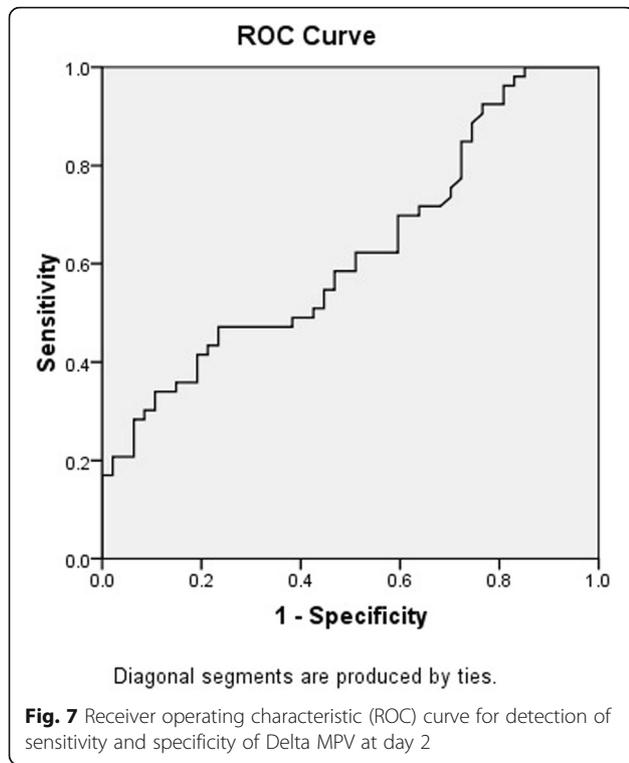
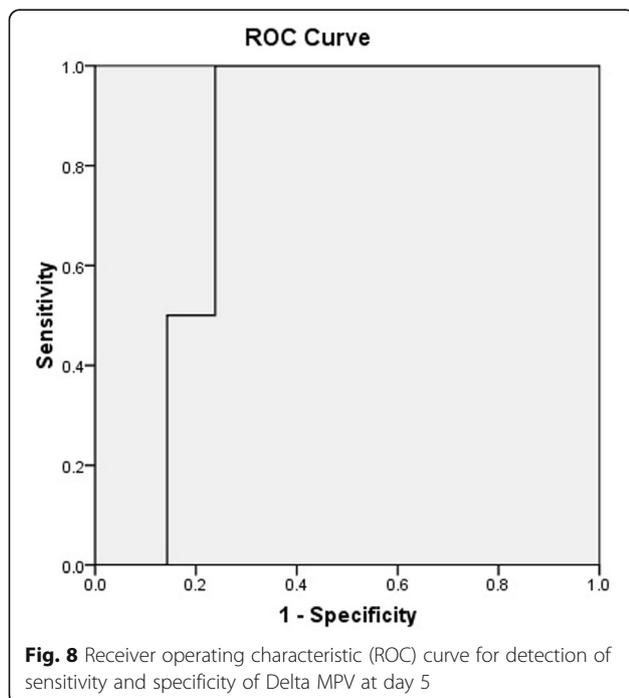


Fig. 6 Percentage changes in MPV (Delta MPV) among ICU complicated versus non-complicated patients during the 1st week of ICU stay. Data presented as means, and error bars represent standard deviation. The asterisk (*) indicates significant difference of Delta MPV between complicated and non-complicated cases



Although there are some contradictory observations as Becchi et al. (2006), who evaluated the impact of MPV and platelet count on the prognosis of critically ill septic patients and concluded that lower MPVs on admission associated with increased mortality. They reported a



three times increase in death probability of patients with $MPV < 9.7$ fl at the recruitment time. This contradiction can be explained in part by the limited size of the Becchi's study population which could not be adequately represented and in part probably also by the differences in included patients' conditions. Yilmaz, Kara, Gumusdere, Arslan, and Ustebay (2015) stated that MPV and other platelet indices would not help to separate true appendicitis from suspected appendicitis.

The present study has some limitations as the lack of mortality cases that made the comparison very difficult among the study patients. Therefore, further research is required to determine the precise mechanisms underlying the association between MPV and mortality in critically ill patients in pediatric surgical ICU. We also recommend performing further multicenter studies and investigating its prognostic role in comparison with PELOD and PIM scores.

Conclusion

Mean platelet volume (MPV) dynamics and platelet count have a prognostic role and worth value for determining several complications in the critically ill pediatric surgical patients. However, platelet count seemed to be a more specific and sensitive tool to detect complications higher than MPV dynamics. MPV should be used in combination with other prognostic tests to achieve a better outcome for children in pediatric ICU.

Abbreviations

CBC: Complete blood count; MPV: Mean platelet volume; PELOD: Pediatric Logistic Organ Dysfunction Score; PIM: Pediatric Index of Mortality; PLC: Platelet count; PRBCs: Packed red blood cells; PSICU: Pediatric surgical intensive care unit; WBC: White blood cells

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Authors' contributions

HM developed the idea of the study. IA and HM made its design. AG, AE, and HM carried out the implementation, data collection, and analysis and took the lead in writing the manuscript. All authors performed the literature search, manuscript preparation, and revision. All authors read and approved the final manuscript before submission.

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Availability of data and materials

Data supporting findings can be obtained from the corresponding author.

Ethics approval and consent to participate

Local ethics approval committee has been obtained, and written informed consent has been obtained from all parents before the study. This study had been approved by the Research Ethics Committee, Department of Anesthesia, Faculty of medicine, Cairo University.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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