

Mean Platelet Volume and Thrombocytopenia as Hematological Predictive Indicator of Patients' Outcome in Medical Intensive Care Unit

Inayatullah Memon¹ and Hamid Raza²

ABSTRACT

Objective: The present study determined the predictive significance of mean platelet volume (MPV) and low platelet count (thrombocytopenia) as hematological indicator of patient outcome in medical intensive care units (ICU).

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Department of Pathology and Medical ICU, Indus Medical College Hospital, Tando Muhammad Khan, Sindh from April 2017 to March 2019.

Materials and Methods: Critical subjects admitted to medical intensive care units of the hospital were selected according to inclusion and exclusion criteria. A sample of 300 (n=300) patients was selected and analyzed to meet criteria of study. 5-10 ml of venous blood sample was collected for study parameters. Data was analyzed on SPSS 21.0 IBM, Incorporation USA at 95% confidence interval.

Results: Thrombocytopenia was noted in 70 (23%) and severe thrombocytopenia in 19 (6.3%) patients (P=0.0001). Thrombocytopenia and severe thrombocytopenia were noted in 14 (4.6%) of non- survivors vs. (1.6%) in survivors (P=0.0001). Normal and elevated MPV in survivors and non- survivors were noted in 195 (65%) vs. 40 (13.3%) and 14 (4.6%) vs. 51 (17%) respectively (P=0.0001). Platelet counts and MPV in survivors and non- survivors were noted as 378457±459 vs. 123153±366 (x10⁹/L) (P=0.0001) and 9.83±1.23 vs. 14.73±3.53 fl respectively (P=0.0001). ROC curve shows area under curve (AUC) of 0.913 (91.3%) (P=0.0001).

Conclusion: Thrombocytopenia and elevated MPV are useful hematological indicators to predict the poor patient outcome and mortality.

Key Words: Thrombocytopenia, Mean Platelet Volume, Intensive care unit.

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INTRODUCTION

Thrombocytopenia is a common hematological finding in intensive care units (ICU) admitted patients. Infectious such as the malaria and sepsis and non-infectious agents such as the drugs are known causative agents.¹ In addition to the platelet counts, the mean platelet volume (MPV) has currently researched parameter of prognostic significance in ICU patients.¹⁻³ MPV is a measure of platelet size, function and activation.³

In pathological conditions of accelerated platelet consumption, the MPV is found elevated. When platelets are consumed rapidly, it results in low platelet counts called the thrombocytopenia. Fresh platelets released from bone marrow in circulation have high MPV. Bone marrow released fresh platelets have large size, more dense granules and are physiologically active. The enzyme systems and metabolic reactions do occur rapidly in young platelets. For example, the content of platelet activator thromboxane A₂ (TxA₂) is very high in young platelets compared to older one. Recently, interest has been seen in research in platelet counts and MPV indices as simple indicators of patient outcome in ICU⁴⁻⁶ and brain stroke and myocardial infarction.⁷ In intensive care units admitted patients, the frequency of thrombocytopenia has been reported in range of 13 - 44%.⁸ Why the frequency of thrombocytopenia is high in intensive care unit admitted patients is not known. It is considered as multi- factorial in ICU setting. In majority of cases, it is not easy to reach to the proper exact cause. Malignancy, invasive catheters, sepsis, and medications such as the cephalosporin have been reported as causative agents of thrombocytopenia. Heparin, an anticoagulant, is a

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common cause of thrombocytopenia. This is called the heparin- induced thrombocytopenia (HIT). Many confounding factors are working together; hence pointing out the exact cause of thrombocytopenia is a challenging job. Thrombocytopenia and elevated MPV have been linked to high mortality in critically ill ICU patients.^{1,8,9} Platelet count $<150 \times 10^9/L$ is termed as thrombocytopenia; however; for ICU settings the cut point $<100 \times 10^9/L$ is considered as thrombocytopenia. Platelet counts $<50 \times 10^9/L$ is termed as severe thrombocytopenia.^{9,10} Because of bleeding tendency and thrombosis, the platelet counts considered a marker of survival and mortality among ICU patients.^{11,12} In critically ill ICU patients, the thrombocytopenia may cause bleeding, organ failure and mortality.^{10,13,14} A Korean study recently reported on the thrombocytopenia in the ICU as marker of poor patient outcome.¹⁵ A few studies are available from developing countries such as Pakistan. This prompted the researchers to analyze the frequency of thrombocytopenia and mean platelet volume (MPV) in critically ill ICU patients and their effects on the patient outcome in medical intensive care units at our tertiary care hospital.

MATERIALS AND METHODS

The present observational study was conducted at the Department of Pathology and medical ICU, Indus Medical College Hospital, Tando Muhammad Khan, Sindh. The study covered duration of 2 years from April 2017 to March 2019. Critical subjects admitted to medical intensive care units of the hospital were selected according to inclusion and exclusion criteria. Both male and female, adult age and suffering from sepsis were included. Those having history of aspirin intake, smoking and in moribund condition were excluded. A sample of 300 patients was selected and analyzed to meet criteria of study. Patients were divided into 2 groups according to the platelet counts. Group 1- was defined as normal platelet counts (normo-thrombocytosis) and Group 2- was defined as low platelet counts (thrombocytopenia). Subjects who meet the inclusion and exclusion criteria were studied. Written consent was taken from the legal heirs of the patients. They were informed that the study will never inflict damage, even a tiny damage, to the patient. Self-willing volunteers were included in the study protocol. A signed consent was taken on a proforma in writing. Biodata of patients were taken including drug history. Medical history was asked by a medical officer and recorded in a pre- structured proforma. Medical officers strictly followed the inclusion and exclusion criteria. Participants were finally examined by a Consultant Physician. 5-10 ml of venous blood sample was collected from each participant. Age, gender distribution, body weight, BMI and systemic blood pressure were noted. Blood glucose, hemoglobin blood

urea nitrogen (BUN) and serum creatinine were detected by standard methods by a Consultant Pathologist. Blood glucose was estimated by "hexokinase" method. Blood was analyzed on hematology analyzer. Platelet counts $>150 \times 10^9/L$ was defined as normo-thrombocytosis and $<150 \times 10^9/L$ was termed the thrombocytopenia. For ICU settings the cut point of thrombocytopenia was taken at $<100 \times 10^9/L$. Platelet counts $<50 \times 10^9/L$ was defined as severe thrombocytopenia. Normal mean platelet volume (MPV) was taken as 8.5 – 11.5 fl.^{9,10} Institute's ethical permission was taken in writing. Confidentiality of patients Biodata and laboratory findings was maintained by keeping the record in lockers. Data was analyzed on SPSS 21.0 IBM, Incorporation USA. Statistical comparison between groups was carried by Student's t-test (numerical data) and Chi square test (categorical data). 95% confidence interval ($P \leq 0.05$) was taken statistically significant.

RESULTS

Demography characteristics of study subjects are shown in table 1. Age, gender distribution, body weight, BMI, hemoglobin and systemic blood pressure shows non-significant differences between Normo-thrombocytosis and thrombocytopenic subjects ($P > 0.05$). Blood glucose, blood urea nitrogen (BUN) and serum creatinine differed significantly between Normo-thrombocytosis and thrombocytopenic subjects ($P < 0.05$). Platelet counts and MPV differed significantly between survivors and non- survivors ($P < 0.05$) as shown in table 2, 3 and 4.

Table No.1: Characteristics and laboratory findings of study subjects (n=300)

	Group 1. Normo- thrombocytosis (n=230)	Group 2. Thrombocytopenia (n=70)	P-value
Age (years)	51.7±9.6	51.7±9.6	0.091
Male	123 (%)	37 (%)	0.078
Female	107 (%)	33 (%)	
Body wt. (kg)	83.5±12.5	84.3±13.7	0.90
BMI (kg/m ²)	30.67±3.45	29.7±4.5	0.93
Systolic BP (mmHg)	130.4±19.3	126.3±17.5	0.97
Diastolic BP (mmHg)	76.6±11.5	79.0±13.3	0.89
Blood Glucose (R) (mg/dl)	120.3±13.2	139.01±29.3	0.049
BUN (mg/dl)	11.9±0.73	15.03±0.70	0.023
Serum creatinine (mg/dl)	3.03±1.23	1.2±0.09	0.003
Hemoglobin (g/dl)	13.03±1.03	12.98±1.09	0.059
Platelet Counts ($\times 10^9/L$)	423457±256	70457±457	0.0001
MPV (fl)	10.3 ±1.45	15.73±3.23	0.0001

Normo-thrombocytosis and thrombocytopenia were noted in 230 (77%) and 70 (23%) of total 300 subjects respectively (P=0.0001). Of 70 patients, the severe thrombocytopenia was noted in 27% (n=19) patients.

Table No.2: Platelet counts among survivors and non- survivors (n=300)

	Survivors	Non-Survivors	Total	p-value
Normo-thrombocytosis	197 (65.6%)	33 (11%)	230 (77%)	0.0001
Thrombocytopenia	33 (11%)	18 (6%)	51 (17%)	
Severe thrombocytopenia	5 (1.6%)	14 (4.6%)	19 (6.0%)	
Total	235 (%)	65(%)	300 (100%)	

Table No.3: MPV among survivors and non-survivors (n=300)

	Survivors	Non-Survivors	Total	p-value
Normal MPV	195 (65%)	40 (13.3%)	235 (78.3%)	0.0001
Elevated MPV	14 (4.6%)	51 (17%)	65 (21.6%)	
Total	209 (69.9%)	91 (30.3%)	300 (100%)	

Table No.4: Platelet counts and MPV among survivors and non- survivors (n=300)

	Survivors	Non-Survivors	p-value
Platelet counts	378457±459	123153±366	0.0001
MPV	9.83±1.23	14.73±3.53	0.0001

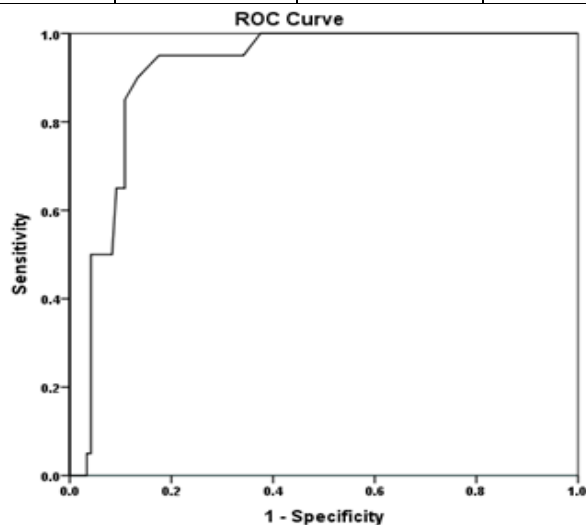


Figure No.1 Reciever Operating Characteristic curve as model of predictive.

Table No.5: Area Under the Curve

Test Result Variable(s):		Predicted probability		
Area	Std. Error ^a	P-value ^b	95% Confidence Interval	
			Lower Bound	Upper Bound
0.913	0.026	0.0001	0.762	0.964

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Platelet counts in normo-thrombocytosis and thrombocytopenic were noted as 423457±256 and 70457±457 (x10⁹/L) respectively (P=0.0001). Mean platelet volume (MPV) in normo-thrombocytosis and thrombocytopenic was noted 10.3 ±1.45 and 15.73±3.23 fl respectively (P=0.0001) (table 4). Logistic regression model of MPV prediction of patient survival is shown in table 5. ROC curve shows area under curve (AUC) of 0.913 (91.3%) and highly significant P value (P=0.0001).

DISCUSSION

The present study determined the predictive significance of mean platelet volume (MPV) and low platelet count (thrombocytopenia) as a marker of patient outcome in medical intensive care units. The present study reports the thrombocytopenia and MPV as possible hematological indicator of patient outcome prognosis in ICU patients. The findings are in agreement with previous studies.^{1,2, 8,9} Above studies^{1,2, 8,9} reported the prognostic significance of thrombocytopenia. They reported that the thrombocytopenia is associated with increased mortality in ICU patients irrespective of the cause. In present study, thrombocytopenia was noted in 70 (23%) out of 300 subjects (P=0.0001) and severe thrombocytopenia in 19 (6.3%) patients (P=0.0001). Thrombocytopenia and severe thrombocytopenia were noted in 14 (4.6%) of non- survivors vs. (1.6%) in survivors (P=0.0001). The findings are in agreement with previous reported frequency of 13 - 44%.⁸ However, Fadaei et al² detected thrombocytopenia in 35% of patients that is inconsistent to present and previous studies.⁸ Thiery-Antier et al reported thrombocytopenia in 48.4% patients and severe thrombocytopenia (platelet count <50 × 10⁹/l) in 14.8% patients.¹⁶ Findings of Thiery-Antier et al¹⁶ are discordant to the present study; as thrombocytopenia was noted in 23% and severe thrombocytopenia in 19 (27%) patients. In present study, the Platelet counts in normo-thrombocytosis and thrombocytopenic were noted as 423457±256 and 70457±457 (x10⁹/L) respectively. The findings are in agreement with previous studies.¹⁷⁻¹⁹ that have reported platelet counts of similar range. In present study, the MPV was elevated to 15.73±3.23 fl in thrombocytopenic patients. Normal and elevated MPV in survivors and non-

survivors were noted in 195 (65%) vs. 40 (13.3%) and 14 (4.6%) vs. 51 (17%) respectively (P=0.0001). Platelet counts and MPV in survivors and non-survivors were noted as 378457 ± 459 vs. 123153 ± 366 ($\times 10^9/L$) (P=0.0001) and 9.83 ± 1.23 vs. 14.73 ± 3.53 fl respectively (P=0.0001). ROC curve shows area under curve (AUC) of 0.913 (91.3%) (P=0.0001). Logistic regression model shows high predictive value of MPV as marker of non-survivor (AUC=0.913) (P=0.0001). Elevated MPV of present study is in agreement with previous studies.³⁻⁷ The study by Kucukardali et al⁷ reported high MPV in ICU patients; however, they concluded that the MPV was not predictable of mortality that is in disagreement to present and previous studies.^{2,7,8} Huczek et al¹⁷ reported that the MPV was elevated in patients and correlated with age and hypertension in ICU patients. The finding of elevated MPV is in full agreement with the present study. Nalbant et al¹⁸ reported the MPV was elevated in variceal upper gut bleeding but the correlation was not found. Again, the finding of elevated MPV is in agreement to the present study. The present study included heterogeneous group of patients. To the best of knowledge, the present study is first time reporting on the thrombocytopenia and MPV from Pakistan in the ICU patients. We detected significant difference in thrombocytopenia and MPV values between the ICU survivors and non-survivors. MPV has emerged as a predictive risk factor for myocardial infarction and brain stroke¹⁹ and sepsis.²⁰ Kisacik et al²¹ reported the MPV values were high in active ankylosing spondylitis and rheumatoid arthritis patients compared to controls. Coban et al²² reported elevated MPV in familial Mediterranean fever (FMF) and concluded the MPV may indicate the increasing risk atherosclerotic in FMF patients. Yilmaz et al²³ reported that the platelet indices including MPV are of diagnostic and prognostic value in animals and humans beings with endotoxemia. Becchi et al²⁴ reported that the platelet count and MPV showed a correlation with during the course of sepsis when expressed as means and frequency distributions. We conclude that the low platelet count (thrombocytopenia) and elevated MPV may help to predict the patient outcome in ICU settings. The present study is a unique contribution to the medical literature that demands more future studies with large sample size. The limitations of present study are a small sample size, heterogeneous patients belonging to peculiar ethnicity, hence results cannot be generalized. We suggest both thrombocytopenia and high MPV may be used as a easy and inexpensive hematological predictive indicator of patient outcome in ICU patients.

CONCLUSION

Mean platelet volume and thrombocytopenia are the common hematologic abnormalities that might be considered as a prognosis monitor of patients' outcome

in ICU settings. Severe thrombocytopenia with elevated mean platelet volume may be useful indicator of poor prognosis and mortality. The simple, effortless and cost-effective hematological findings of platelet count and mean platelet volume should be extensively investigated to predict severity of the critical illness and patients' outcome in medical intensive care units.

Author's Contribution:

Concept & Design of Study: Inayatullah Memon
 Drafting: Hamid Raza
 Data Analysis: Hamid Raza
 Revisiting Critically: Inayatullah Memon
 Final Approval of version: Inayatullah Memon

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