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Association of Admission Platelet Crit with In-Hospital Outcomes in Non ST-Elevation Myocardial Infarction (NSTEMI)

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ABSTRACT

Objective: To determine the association of admission plateletcrit with in-hospital outcomes in non ST-elevation myocardial infarction (NSTEMI).

Study Design: Analytical Cross-sectional study

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi; from Nov 2023 to Apr 2024

Methodology: Using non-probability consecutive sampling, 270 patients were included in this study. ECG findings were noted. Patients were divided into three tertiles based upon plateletcrit value such as T1=lower than normal PCT value (<0.21), T2=normal PCT(0.21-0.22) and T3= higher than normal PCT value (>0.22). PCT values were obtained from complete blood count sent at the time of presentation to AFIC emergency using Mandray BC 6200 CBC analyzer available at the AFIC pathology laboratory.

Results: The study included 270 patients, out of which 137(50.7%) were males and 133(49.3%) were females and median age was 62.00(55.00-70.00) years. T1, T2 and T3 had 71(26.3%), 34(12.6%) and 165(61.1%) patients, respectively. Significant frequency differences of hypertensive and hyperlipidemia patients, and in-hospital outcomes were found between tertiles (p<0.01). Plateletcrit value was identified as an independent predictor for in-hospital outcomes including coronary revascularization (OR=0.08, 95% CI: 0.04-1.58, *p*<0.01), cardiogenic shock (OR=0.24, 95% CI: 0.15-0.37, *p*<0.01) and mortality (OR=0.04, 95% CI: 0.02-0.11, *p*<0.01), when adjusted for covariates.

Conclusion: Plateletcrit value is an important predictor of in-hospital outcomes in NSTEMI patients, particularly coronary revascularization, cardiogenic shock, and mortality.

Keywords: In-hospital outcomes, Non-ST elevation myocardial infarction, Plateletcrit, Platelet indices.

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INTRODUCTION

Acute coronary syndrome (ACS) refers to a group of conditions that include ST-elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina. Coronary heart diseases affected about 3.8 million people in South Asia in 2021.[1]

Platelets are critical in both the initiation and progression of ACS.[2] They play a key role in maintaining homeostasis and angiogenesis. Platelet activation can lead to atherothrombosis, vascular occlusion, and acute ischemic episodes, triggering ACS.[3,4] Commonly evaluated platelet parameters include mean platelet volume (MPV) and plateletcrit (PCT), which may have prognostic and predictive value in inflammatory conditions.[3] PCT, in particular, offers insights into total platelet mass and has independent predictive value for long-term mortality and major adverse cardiac events (MACE).[5]

Patients with high PCT significantly show MACE, hospitalization for heart failure and the incidence of reinfarction. Other platelet indices like MPV on admission to the hospital is a strong and independent predictor of impaired reperfusion and mortality in STEMI patients treated with primary percutaneous coronary intervention (PPCI).[6]

Unstable angina and NSTEMI are initially difficult to tell apart, PCT will assist to make a confirmed diagnosis. This simple tool may also be used to predict in-hospital outcomes in patients presenting with NSTEMI.[5] Pakistan has a higher incidence of CHD particularly NSTEMI and it adds to the morbidity and mortality in general population. A research done in Pakistan by Ali *et al.*, gave a proportion of NSTEMI patients as 18.6%.[7] The high prevalence of NSTEMI, highlights the utmost importance to understand the role of admission plateletcrit. PCT may serve as a simple, effective

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biomarker for diagnosing NSTEMI and predicting in-hospital outcomes, thereby enhancing patient management and outcomes in a region with significant cardiovascular disease burden. Thus, the study aimed to determine the association of admission plateletcrit with in-hospital outcomes in NSTEMI patients.

METHODOLOGY

This was an analytical cross sectional study, carried out over a time period of six months (November 2023 - April 2024) at Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi after the approval from Institutional Ethical Review Board (IERB) (Letter #9/2/R&D/2023/289, Dated: 06th November, 2023)

The sample of 233 was calculated by WHO sample size calculator, by using 18.6% proportion of NSTEMI patients,[7] keeping confidence level of 95% and 5% margin of error. However, we collected data from 270 patients.

Inclusion Criteria: Study participants were NSTEMI patients regardless of gender and aged > 18 years.

Exclusion Criteria: Patient who presented with congestive cardiac failure, history of PCI, Coronary Artery Bypass Grafting (CABG), valvular heart diseases, Chronic Obstructive Pulmonary Disease (COPD), inflammatory diseases, infectious diseases, peripheral arterial disease, pregnant females and patients with recent blood transfusion were excluded.

After taking informed consent from 270 study participants who satisfied the inclusion and exclusion criteria and enrolled by using non-probability consecutive sampling, data was collected on data collection tool. Data collection tool had the essential information like patient's history and laboratory investigations, patients' demographics, comorbid, symptoms and ECG findings were noted. PCT values were obtained from complete blood count sent at the time of presentation to AFIC emergency department using Mandray BC 6200 CBC analyzer available at the pathology laboratory of AFIC. Normal range of PCT value used was 0.21-0.22%.[8,9] PCT was defined as the total platelet mass, which was calculated by using following formula;

PCT = Platelet Count × MPV / 10,000

NSTEMI was diagnosed after analyzing patient's clinical presentation, ECG analysis and Trop-I levels. In-hospital outcomes were assessed for admitted NSTEMI patients. They were divided into three tertiles based upon PCT value as Tertile 1; lower than normal PCT value (<0.21), Tertile 2; normal PCT value (0.21-0.22) and Tertile 3; higher than normal PCT value (>0.22).[10]

For data analysis, statistical software Statistical Package for Social Sciences (SPSS) 27:00 was used. Mean/standard deviation or Median(IQR) were calculated according to the data normality checked by Shapiro-Wilk test, to present quantitative variables like age, MPV, PCT, while qualitative data was presented as frequency and percentage like gender, and in hospital outcomes. The Pearson Chi-Square test was used to determine associations of categorical variables with tertiles, while one-way ANOVA/Kruskul Wallis test was employed to assess mean differences of continuous variables among tertiles and p-value≤0.05 was taken as statistically significant. Risk stratification was done by binary logistic regression analysis to check the independent effect of admission PCT on in hospital outcomes in NSTEMI patients

RESULTS

A total of two hundred and seventy patients were included in this study, out of which 137(50.7%) were males and 133(49.3%) were females, age ranged from 28-82 years. About 71(26.3%) patients had lower plateletcrit value (tertile-1), 34(12.6%) were in tertile-2 with normal plateletcrit value and 165(61.1%) had high plateletcrit value (tertile-3). Majority of the patients were hypertensive and active smokers [188(69.6%), 139(51.5%)] respectively. Overall median of PCT of all study participants was higher than normal range [Median(IQR): 0.25(0.20-0.30), while MPV and platelet count were within normal range. (Table-I).

Table-I: Demographics, Comorbids and Platelet Indices of Study Participants (n=270)

Baseline Characteristics			Median (IQR)
Demographics	Age (years)		62.00(55.00-70.00)
			Frequency (%)
	Gender	Male	137(50.7%)
		Female	133(49.3%)
Comorbids	Diabetes Mellitus		109(40.4%)
	Hypertension		188(69.6%)
	Smoking		139(51.5%)
	Hyperlipidemia		77(28.5%)
			Median (IQR)
Platelet Indices	Platelet Count (x10^3)		219.00(177.00-305.00)
	Platelet Crit (%)		0.25(0.20-0.30)
	Mean Platelet Volume (fL)		10.90(10.10-11.50)

Majority of the patients 159(58.9%) underwent coronary revascularization followed by LVF and cardiogenic shock [79(29.2%), 75(27.8%)] respectively and mortality was reported in 53(19.6%) of the total study subjects as shown in Figure-1.

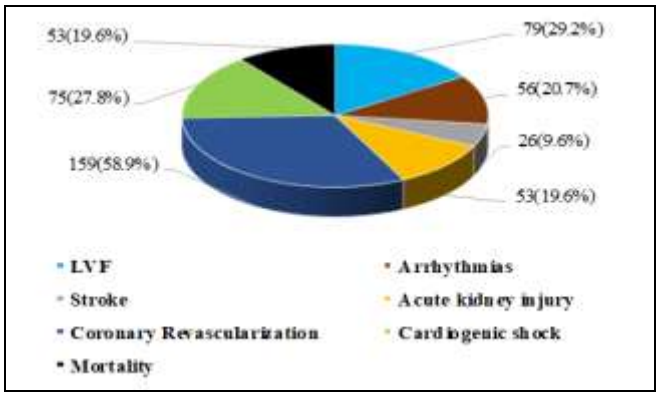

Figure-1: Frequency of In-Hospital Outcomes (n=270)

Table-II depicted significantly greater number of hypertensive and hyperlipidemia patients in tertile-3 in comparison to tertile-1 and tertile-2 (83.6% vs 47.9% and 83.6% vs 47.1%; p<0.01) respectively. Association was not significant for demographics and other comorbids (p>0.05), however comparatively greater percentage of diabetics and smokers can be noted in tertile-3 (45.5% and 54.4%) respectively. Median values of MPV, platelet count and PCT were significantly different across three tertiles (p<0.05). In addition, there exists a statistically significant (p<0.01) frequency difference of in-hospital outcomes in tertiles with greater percentages noted in tertile-3 except coronary revascularization that was noted in 52(73.2%) out of 71 patients of tertile-1.

The key findings according to table-III indicate that Plateletcrit value was identified as an independent predictor for in-hospital outcomes including coronary revascularization (OR=0.08, 95% CI: 0.04-1.58, p<0.01), cardiogenic shock (OR=0.24, 95% CI: 0.15-0.37, p<0.01) and mortality (OR=0.04, 95% CI: 0.02-0.11, p<0.01), when adjusted for covariates.

DISCUSSION

This study mainly focused on in-hospital outcomes recorded in NSTEMI patients and association with PCT. As the PCT was divided into three tertiles, Tertile-3 had higher value and it was associated with more severe outcomes, while lower PCT was associated with better prognosis (p<0.05). The in-hospital outcomes included coronary revascularization, LVF, arrhythmias, stroke, acute kidney injury, cardiogenic shock and mortality. PCT value was identified as an independent predictor for coronary revascularization, cardiogenic shock and, mortality when adjusted and unadjusted for covariates (p<0.05).

In ACS, a thrombogenic environment develops around atherosclerotic plaques which may lead to adverse clinical outcomes.[11] The thrombus that is formed on a damaged endothelium of vessel can enlarge after rupture of plaque and its erosion.[12] This event leads to a prothrombotic state and an inflammatory response ensues. The inflammatory response and prothrombotic state are involved in the development of ACS.[13,14] Markers of inflammatory and thrombotic activity may reflect the severity of ACS and may predict the occurrence of MACE. Platelet indices like MPV and PCT are some of the important markers of prothrombotic activity and inflammation.[2,4,15,16]

In the current study, the mean age of participants was 61.54±11.03 years, which is consistent with previous findings from both a national study in Pakistan,[10] reporting a mean age of 59.75±8.60 years, and an international study,[14] where the mean age was 59.2±11.8 years. These consistent age ranges, suggest that NSTEMI patients generally belong to older demographic. In a similar study from Pakistan,[15] the mean PCT value was reported as 0.28±0.06%, and the mean MPV value was 9.06±0.64 fL. Comparatively, in our study, the median PCT was 0.25(0.20-0.30)% and the mean MPV was 10.90(10.10-11.50) fL. The close alignment of PCT values across studies highlights the clinical relevance of PCT as a biomarker in this patient population. Moreover, the higher mean MPV in our study may reflect differences in patient characteristics or disease severity, providing further insight into platelet activity in NSTEMI patients. Thus, the findings highlight the significance of study in contributing in the growing body of evidence on prognostic utility of PCT and MPV in NSTEMI management.

An earlier study by Bećirović et al. revealed that high MPV has a strong and independent association with an increased risk of plaque rupture in NSTEMI patients.[17] Similar results were noted in our study group having high PCT value (p=0.01). The measured results in our study [Median MPV: 10.90(10.10-11.50)] are in tune with a previous study which depicted MPV (8.78±1.38) to be a strong predictor of NSTE-ACS.[2] The MPV similar to PCT is strongly associated with

atherothrombosis and thus ACS, as the previous study explained an association between higher MPV and NSTEMI, this is clearly indicated in our study as well. Acute myocardial infarction was found to be more common in patients with greater PCT (0.30±0.04), according to a recent study by Tasneem.[18] This was consistent with the findings of our investigation, which showed greater percentage of in-hospital outcomes in tertile-3 having median PCT 0.29(0.25-0.35). Acute myocardial infarction includes both ST elevation myocardial infarction and NSTEMI. The mentioned study included both group of patients and both groups had a greater value of PCT. Our study focused on NSTEMI only and didn't include STEMI patients.

In another study by Kathrine *et al.,* it was found that higher PCT value is correlated with worse cardiovascular outcomes including cardiogenic shock in patients of coronary heart diseases.[19] In our study, we observed PCT was found to be predictor of cardiogenic shock(p=0.001). Higher in-hospital outcomes like Acute kidney injury (p=0.001) cardiogenic shock (p=0.001) coronary revascularization (p=0.003) mortality (p=0.001) were observed in tertile-3 of our study. This is in accordance with previous studies where in-hospital outcomes like Acute kidney injury (p=0.027), cardiogenic shock (p<0.001) target lesion revascularization (p=0.001) and all-cause mortality (p<0.001) were significantly greater in tertile-3 where PCT was of higher value.[8]

Table-II: Association of Demographics, Clinical Characteristics, and In-Hospital Outcomes with Tertiles (n=270)

Variables		T1 (<0.21) (Total=71)	T2 (0.21-0.22) (Total=34)	T3 (≥0.23) (Total=165)	*p*-value
Demographics					
Age(years) (Mean±SD)		63.00(52.00-71.00)	59.00(50.00-63.00)	62.00(55.00-71.00)	0.09
Comorbids [Frequency(%)]					
Gender	Male	40(56.3%)	16(47.1%)	81(49.1%)	0.54
	Female	31(43.7%)	18(52.9%)	84(50.9%)	
Diabetes Mellitus	Yes	24(33.8%)	10(29.4%)	75(45.5%)	0.09
	No	47(66.2%)	24(70.6%)	90(54.5%)	
Hypertension	Yes	34(47.9%)	16(47.1%)	138(83.6%)	0.001
	No	3(52.1%)	18(52.9%)	27(16.4%)	
Smoking	Yes	34(47.9%)	15(44.1%)	90(54.5%)	0.41
	No	37(52.1%)	19(55.9%)	75(45.5%)	
Hyperlipidemia	Yes	9(12.7%)	4(11.8%)	64(38.8%)	0.001
	No	62(87.3%)	30(88.2%)	101(61.2%)	
Laboratory findings					
Mean Platelet Volume(fL)		11.40(10.20-11.90)	11.10(9.80-12.00)	10.70(9.91-11.30)	0.013
Platelet count (cells/x10^3 uL)		156(132-177)	195(162-206)	275(227-337)	0.001
Plateletcrit value (%)		0.17(0.16-0.18)	0.22(0.21-0.22)	0.29(0.25-0.35)	0.001
In-Hospital Outcomes [Frequency(%)]					
LVF	Yes	10(14.1%)	6(17.6%)	63(38.2%)	0.001
	No	61(85.9%)	28(82.4%)	102(61.8%)	
Arrhythmias	Yes	10(14.1%)	2(5.9%)	44(26.7%)	0.007
	No	61(85.9%)	32(94.1%)	121(73.3%)	
Acute kidney injury	Yes	2(2.8%)	2(5.9%)	49(29.7%)	0.001
	No	69(97.2%)	32(94.1%)	116(70.3%)	
Coronary Revascularization	Yes	52(73.2%)	23(67.6%)	84(50.9%)	0.003
	No	19(26.8%)	11(32.4%)	81(49.1%)	
Stroke	Yes	2(2.8%)	-	24(14.5%)	0.003
	No	69(97.2%)	34(100%)	141(85.5%)	
Cardiogenic shock	Yes	6(8.5%)	4(11.8%)	65(39.4%)	0.001
	No	65(91.5%)	30(88.2%)	100(60.6%)	
Mortality	Yes	-	1(2.9%)	52(31.5%)	0.001
	No	71(100%)	33(97.1%)	113(68.5%)	

LVF=Left Ventricular Failure

Table-III: Covariates of In-hospital Outcomes (n=270)

Covariates for Coronary Revascularization			Univariate logistic regression			Multivariate logistic regression		
			***p*-Value**	**uOR**	**95%CI for uOR**	***p*-Value**	**aOR**	**95%CI for aOR**
PCT value(%)			0.001	2.26	1.65-3.11	0.009	0.08	0.04-1.58
Age(years)			0.20	1.02	0.99-1.03			
DM	Yes	109(40.4%)	0.02	0.46	0.28-0.75	0.02	0.52	0.30-0.90
	No	161(59.6%)						
HTN	Yes	188(69.6%)	0.01	0.34	0.19-0.61	0.03	0.51	0.28-0.96
	No	82(30.4)						
Smoking	Yes	139(51.5%)	0.97	1.009	0.62-1.63	-	-	-
	No	131(48.5%)						
Hyperlipidemia	Yes	77(28.5%)	0.71	1.10	064.-1.88	-	-	-
	No	193(71.5%)						
MPV(fL)			0.05	0.75	0.61-0.91	0.21	1.55	0.77-3.08
Platelet count (cells/uL)			0.001	1.00	1.00-1.00	0.03	1.00	1.00-1.00
Covariates for Cardiogenic Shock			***p*-value**	**uOR**	**95%CI for uOR**	***p*-value**	**aOR**	**95%CI for aOR**
PCT value(%)			0.001	0.22	0.15-0.34	0.001	0.24	0.15-0.37
Age(years)			0.03	0.96	0.93-0.99	0.006	0.95	0.92-0.98
DM	Yes	109(40.4%)	0.06	1.66	0.97-2.84	-	-	-
	No	161(59.6%)						
HTN	Yes	188(69.6%)	0.09	1.70	0.92-3.16	-	-	-
	No	82(30.4)						
Smoking	Yes	139(51.5%)	0.23	1.38	0.81-2.37	-	-	-
	No	131(48.5%)						
Hyperlipidemia	Yes	77(28.5%)	0.001	2.93	1.66-5.16	0.05	1.90	0.97-3.71
	No	193(71.5%)						
MPV(fL)			0.005	1.38	1.10-1.74	0.08	1.25	0.97-1.61
Platelet count (cells/uL)			0.001	1.00	1.00-1.00	-	-	-
Covariates for Mortality			***p*-value**	**uOR**	**95%CI for uOR**	***p*-value**	**aOR**	**95%CI for aOR**
PCT value(%)			0.001	0.06	0.03-0.12	0.001	0.04	0.02-0.11
Age(years)			0.06	0.97	0.94-1.00	-	-	-
DM	Yes	109(40.4%)	0.01	2.06	1.12-3.79	0.98	1.01	0.39-2.56
	No	161(59.6%)						
HTN	Yes	188(69.6%)	0.002	0.23	1.72-10.3	0.91	0.93	0.30-2.88
	No	82(30.4)						
Smoking	Yes	139(51.5%)	0.93	0.97	0.53-1.77	-	-	-
	No	131(48.5%)						
Hyperlipidemia	Yes	77(28.5%)	0.008	2.31	1.24-4.32	0.88	1.07	0.41-2.77
	No	193(71.5%)						
MPV(fL)			0.001	1.68	1.26-2.23	0.001	1.93	1.28-2.91
Platelet count (cells/uL)			0.001	1.00	1.00-1.00			

aOR= Adjusted Odds Ratio; uOR=Unadjusted Odds Ratio; DM=Diabetes Mellitus; HTN= Hypertension; MPV= Mean Platelet Volume; PCT= Plateletcrit

Furthermore, Kathrin *et al.*,[19] reported 58 patients in the MACE group and 116 in the non-MACE group for ACS. Among the MACE group, 25 patients died from cardiac arrest, 24 from cardiogenic shock, 4 from lethal arrhythmias, 2 experienced re-infarction, and 3 had strokes. These findings align with our study, which involved a larger population (n=270). In our study, 75 patients experienced cardiogenic shock, 56 had arrhythmias, 26 had strokes, and 53 deaths were recorded. The in-hospital outcomes in our study reflect our hospital's administrative policy of admitting MACE patients to the coronary care unit, while NSTEMI patients without MACE are sent to the catheterization lab and PCI unit immediately post-revascularization.

In a past research work carried out by Sudharsono *et al.*,[20] demonstrated elevated PCT as a strong predictor of mortality in ACS patients, with

46% of non-ST elevated ACS (NSTE-ACS) cases showing a significant association (OR: 2.6, p<0.001), that reflects the prognostic importance of PCT. In current study findings mortality was also significantly associated with PCT tertiles and 52(31.5%) mortality cases out of 165 had elevated PCT (tertile-3). Additionally, the elevated MPV values observed in our study align with findings from an Indian study,[21] where MPV was significantly higher in patients with myocardial infarction and unstable angina compared to those with stable angina (p<0.001). This signifies the clinical relevance of PCT and MPV in identifying high-risk ACS patients and guiding treatment decisions.

When 5-year long-term mortality was assessed, results revealed significantly higher mortality in ACS patients with abnormal PCT and MPV levels in comparison to those with normal levels.[22] While our study focused on short-term in-hospital outcomes, including mortality, but similar findings were observed. Our study was conducted over a shorter duration. Moreover, it covered the main clinical outcomes but other clinical outcomes need to be studied as well. Further research with long-term follow-up for MACE is needed to address this issue comprehensively. In patients with NSTEMI undergoing PCI, elevated MPV levels were strongly correlated with a significantly higher incidence of long-term adverse events, particularly all-cause mortality.[23] In acute MI group studied by Khode *et al.*, elevated platelet indices, such as PCT (0.28±0.09%),[24] were observed compared to the control that aligns with our findings [Median PCT: 0.25(0.20-0.30)%)]. This drags the attention to monitor the platelet indices in the management of NSTEMI to save the patients from worse outcomes.

Incorporating PCT as well as MPV into risk stratification models could potentially improve patient outcomes by guiding more personalized post-PCI care strategies. The resources in Pakistan are limited and we have to prioritize patients according to available limited amount of resources. The endpoint is that simple diagnostic parameters like PCT must be implemented in our general practice to predict in-hospital outcomes. Patient who has better prospects of quality of life after coronary revascularization must be referred immediately to advanced cardiac hospital. Moreover, there is a scarcity of studies in Pakistan that highlight PCT as a predictor of in-hospital outcomes in NSTEMI patients. This study filled this gap and made a significant contribution to the literature.

LIMITATION OF THE STUDY

This study lacked long-term follow-up to evaluate clinical outcomes such as arrhythmias, kidney injury, stroke, and left ventricular failure.

CONCLUSION

Our study demonstrated plateletcrit values taken at admission time, to be an important predictor of in-hospital outcomes in NSTEMI patients, particularly coronary revascularization and cardiogenic shock, and mortality. Platelet indices like MPV and plateletcrit can be detected earlier, and are economical, readily available and easily recordable in most clinical laboratories. This makes the indices a potential better marker for these patients.

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Conflict of Interest: None

Authors' Contribution

Following authors have made substantial contributions to the manuscript:

HM & MS: Study concept, study design, drafting the manuscript, approval of the final version to be published

SM & MA: Study concept, data acquisition, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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