International Journal of Research in Medical Sciences
Shanker S et al. Int J Res Med Sci. 2020 Apr;8(4):1404-1413
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20201333

Original Research Article

Usefulness of white blood cell count to mean platelet volume ratio in predicting short term, 30 days major adverse cardiac events in patients presenting with acute coronary syndrome

Sumit Shanker*, Subba Reddy, Ganesan Ramachandran

Department of Cardiology, Mamata Medical College, Khammam, Telangana, India

Received: 13 February 2020
Revised: 16 February 2020
Accepted: 06 March 2020

***Correspondence:**
Dr. Sumit Shanker,
E-mail: sumitshanker123@gmail.com

ABSTRACT

Background: The role of white blood cell (WBC) to mean platelet volume (MPV) ratio (WMR) in predicting short-term major adverse cardiac events (MACE) in patients presenting with acute coronary syndrome (ACS) has not been studied extensively. We aimed to determine whether WMR can predict short-term (30 days) MACE in ACS patients.
Methods: This hospital-based prospective cohort study was undertaken at a tertiary-care teaching hospital in India from January 2018 to December 2018. Fifty patients presenting with ACS to undergo primary percutaneous intervention were evaluated for WMR and short-term MACE.
Results: Receiver operating characteristic (ROC) curve showed cut-off value of WMR as 1059 with area under the ROC curve of 0.825 (SE=0.074; 95% CI: 0.679-0.971; p=0.001). MACE was noted in 10 patients (20%) and mortality in 4 patients (8%). WMR with cut-off value of 1059 was significant and highly accurate in predicting MACE (diagnostic accuracy: 72%, sensitivity: 80%, specificity: 70%, positive predictive value: 40%, negative predictive value: 93.33%, p=0.016, and positive likelihood ratio: 2.67, negative likelihood ratio: 0.29). Risk of short-term MACE increases with higher respiratory rate, creatine kinase and creatine kinase myocardial band, alanine aminotransferase, WBC count, neutrophils, neutrophil to lymphocyte ratio, total bilirubin, aspartate aminotransferase, lymphocytes, uric acid, lower SBP, DBP, Troponin I, red blood cell count, and ejection fraction and clinical presentation such as, palpitations, sweating, giddiness, loss of consciousness, higher Killip class, and diagnosis of inferior wall myocardial infarction.
Conclusions: Higher WMR values on admission (≥1059) are associated with worse short-term outcomes in patients with ACS and independently predict short-term MACE.

Keywords: Acute coronary syndrome, Major adverse cardiac event, White blood cell to mean platelet volume ratio

INTRODUCTION

Acute coronary syndrome (ACS) is a significant contributor to mortality and morbidity attributed to cardiovascular diseases (CVD). It is predicted that more than half the worldwide cardiovascular disease risk burden will be borne by the Indian subcontinent in the next decade, according to a recent epidemiological study.[1] It is a syndrome encompassing unstable angina and both ST segment elevation and non-ST segment elevation myocardial infarction (MI) and is a common cause of emergency hospital admission. Coronary heart disease incidence is increasing in developing countries. However, despite great progress in pharmacotherapy and interventional treatment ACS remains the major cause of mortality and morbidity.[2] The Global Burden of Diseases (GBD) study reported the estimated mortality from coronary artery disease (CAD) in India at 1.6 million in the year 2000. It has been predicted that by the year 2020 there will be an increase by almost 75% in the global

CVD burden. Reddy reported that mortality from CVD was projected to decline in developed countries from 1970 to 2015 while it was projected to almost double in the developing countries.[3] It has been demonstrated that if attention is focused on evidence-based treatments, diagnostic evaluation and processes of inpatient care, desired positive outcome can be achieved.[4]

ACS as a presentation of coronary atherosclerosis is associated with inflammatory mechanisms involved in the development of atherosclerotic plaque and subsequent rupture and thrombosis.[5] Increased white blood cell (WBC) count has been shown to be a predictor of clinical outcomes of patients with ACS.[6] Mean platelet volume (MPV) as a marker of platelet activation is another inflammatory marker that has been demonstrated to be a prognostic marker in ACS setting.[7,8] As a combination of both WBC and MPV, WBC to MPV ratio (WMR) has been recently found as a novel non-invasive marker predicting long-term outcomes in patients with non-ST elevation myocardial infarction (NSTEMI) and in patients with ACS.[9] However, the use of this marker for prognosis in Indian patients with ACS is limited. Therefore, we sought to evaluate whether WMR can be used as a prognostic marker in Indian patients presenting with ACS.

METHODS

This hospital-based prospective cohort study was undertaken at a tertiary-care teaching hospital situated in India from January 2018 to December 2018. Considering the sensitivity of WMR as 69% with mortality rate of 14% based on the study by Adam AM et al, the minimum sample size required was 25 cases with ACS.[10]

Inclusion criteria included patients with ACS. ACS patients were identified by using the following criteria: NSTEMI was confirmed if patients had raised cardiac enzymes without detectable ST-segment elevation on the electrocardiogram (ECG). ST elevation myocardial infarction (STEMI) was confirmed if patient complained of typical chest pain lasting more than 20 min along with any one of the following characteristics: ST-segment elevation of at least 1 mm in two or more contiguous leads, formation of new Q wave or left bundle branch block formation, and/or two times increase in the cardiac enzymes. Unstable angina (UA) was confirmed if there were detectable ischemic changes on an ECG with no increase in cardiac enzymes.[9] Exclusion criteria included age less than 18 years, anticoagulant therapy or an immunosuppressant, conditions exposing the patient to high risk of serious bleeding, diagnosis of cancer, active infectious diseases or inflammatory diseases, or severe liver disease. A total of 50 patients presented with ACS undergoing PCI and fulfilled the selection criterion hence a total of 50 patients were studied. The ethical clearance was obtained from the Institutional Ethics committee prior to the commencement of the study.

Patients who were eligible were briefed about the nature of the study and interventions to be done and written informed consent was obtained. An interviewer-based pilot tested questionnaire was administered to each patient which included demographic data such as age and gender, clinical presentation, history of diabetes mellitus, hypertension, smoking, alcohol consumption and tobacco chewing. A thorough physical examination was conducted to assess the vital parameters. Patients were also evaluated for Killip clinical examination classification and New York Heart Association (NYHA) classification.[11,12]

Laboratory analysis

At baseline, venous blood samples were obtained within 30 min of admission to measure hematological indices and biochemical markers. An automated hematology analyzer SYSMEX XN-1000 was used to measure hematological indices. In addition, detailed liver function tests (LFTS), electrolytes, blood urea nitrogen (BUN) and creatinine (Cr) were measured with Roche Cobas c501 chemistry analyzer (Roche Diagnostics). Fasting lipid panels were measured by standard enzymatic methods. Patients were also evaluated for cardiac ischemia markers, echocardiography and a 12-lead ECG. Troponin I was measured by Chemiluminescence Microparticle Immune-Assay-CMIA (Cobas c601), while other cardiac enzymes were measured by Roche Cobas c501. Left ventricular ejection fraction (LVEF) was assessed by two-dimensional echocardiography. Number of diseased vessel(s) (NODV) was evaluated after patients underwent coronary angiography.

Electrocardiographic and enzymatic analysis

The included patients were subjected to ECG in order to diagnose the type of MI, followed by systemic examination. A standard 12-lead ECG with maximal ST-segment elevation was chosen for measurements. The ECG was recorded at a paper speed of 25mm/sec at a calibration of 1 mV=10 mm. STEMI was diagnosed according to the ESC and ACC criteria as constrictive chest pain lasting longer than 30 min and an increased creatine kinase (CK) (MB-fraction >200 U/l) and/or increased cardiac Troponin I more than 2 microgram\L and/ or new ST elevation at the J point in two contiguous leads >0.2 mV leads v2-v3 or >0.1 mV in other leads).[13,14]

Echocardiography

All included patients were assessed with echocardiography at the time of index hospitalization. The left ventricular end-diastolic diameter was measured from the long axis of the left ventricle, and the left ventricular ejection fraction was calculated using single - plane Simpson's method using two-dimensional echocardiography (ECHO).

Study End Points

Endpoint event was major adverse cardiac events (MACE) one month following discharge, every patient was followed up by administering an interviewer-based, pilot tested questionnaire to record the incidence of MACE. MACE was considered positive if patients had any one of the following events: non-fatal MI, re-hospitalization, cardiac arrhythmias and death. In addition, other adverse events like cardiogenic shock, kidney dialysis, gastrointestinal (GI) bleeding, coronary artery bypass grafting (CABG) and access site complication were also recorded.

Statistical analysis

The data obtained was coded and entered into Microsoft Excel Worksheet. The data was analysed using statistical software SPSS version 20.0. Continuous variables were presented as mean±standard deviation (SD) and analyzed for normality by the Shapiro-Wilk test. Categorical variables were presented as number (percentage) and compared using the Chi-square or Fisher's exact test while continuous variables were compared using Independent t-test or Mann-Whitney U tests. Receiver operating characteristic (ROC) curve analysis was conducted to determine prognostic accuracy of WMR in predicting MACE. The accuracy of WMR in predicting MACE was determined in terms of sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV), and positive and negative likelihood ratios. All tests were two-tailed and a p-value of less than 0.05 was considered significant.

RESULTS

In the present study ROC curve showed cut-off value of WMR as 1059 with area under the curve (AUC) of 0.825 (SE=0.074; 95% CI: 0.679-0.971; p=0.001) (Figure 1). MACE was noted in 10 patients (20%) and mortality was noted in 4 patients (8%). Of the 4 non survivors, 1 case (25%) each had undergone dialysis, cardiac arrhythmias with cardiogenic shock, cardiogenic shock and free wall rupture with cardiac arrhythmias and cardiogenic shock. Among the stable patients the MACE events noted were cardiac arrhythmias in 3 cases (50%), and 1 case each had cardiac arrhythmias with cardiogenic shock, cardiogenic shock and REMI (Table 1).

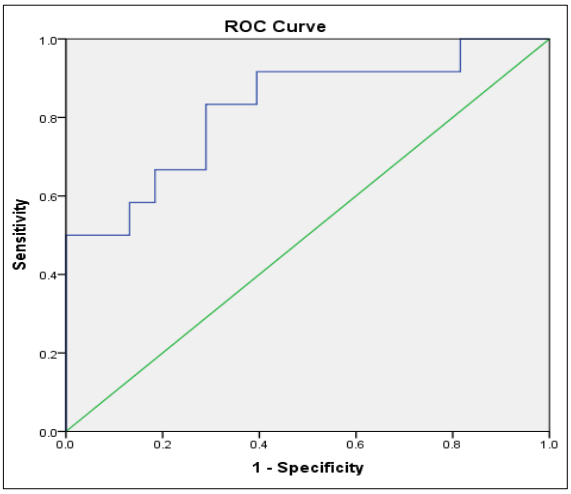

Figure 1: ROC curve showing AUC for WMR in predicting MACE.

Table 1: Distribution of patients according to MACE and WMR.

Parameters	Findings	n (%)
MACE (n=50)	Yes	10 (20%)
	No	40 (80%)
	Total	50 (100%)
Mortality (n=50)	Survivors	46 (92%)
	Non-survivors	4 (8%)
	Total	50 (100%)
MACE with mortality (n=4)	Mortality with dialysis	1 (10%)
	Mortality with cardiac arrhythmias and cardiogenic shock	1 (10%)
	Cardiogenic shock with mortality	1 (10%)
	Mortality with free wall rupture, cardiac arrhythmias and cardiogenic shock	1 (10%)
Other MACE events without mortality (n=6)	Cardiac arrhythmias	3 (50%)
	Cardiac arrhythmias with cardiogenic shock	1 (16.7%)
	Cardiogenic shock	1 (16.7%)
	REMI	1 (16.7%)
	Total	6 (100%)
WMR	High (>1059)	20 (40%)
	Low (≤1059)	30 (60%)
	Total	50 (100%)

MACE-major adverse cardiac events; WMR- WBC count to mean platelet volume ratio

Table 2: Comparison of baseline demographics and risk factors with MACE.

Parameters		MACE		p value
		Present (n=10)	Absent (n=40)	
Age, years (mean±SD)		63.80±15.41	56.53±11.47	0.188
Males, n (%)		7 (24.14%)	22 (75.86%)	0.312
Height, cm		173.10±8.02	168.05±7.64	0.095
Weight, kg		71.90±17.22	66.75±12.57	0.392
Body mass index, kg/m^2		23.67±3.80	23.53±3.48	0.917
Vitals, mean±SD	Pulse rate, per min	89.80±33.22	85.65±17.12	0.914
	Respiratory rate, per min	31.00±6.55	24.45±5.09	0.008
	SBP, mm Hg	104.00±22.21	197.00±326.55	0.009
	DBP, mm Hg	67.00±12.52	80.00±14.32	0.014
Risk factors, n (%)	Prior MI	0 (0%)	3 (100%)	0.504
	Prior PCI	0 (0%)	2 (100%)	0.637
	History of diabetes mellitus	4 (17.39%)	19 (82.61%)	0.474
	History of hypertension	1 (5.88%)	16 (94.12%)	0.073
	History of chronic kidney disease	0 (0 %)	1 (100%)	0.800
	History of hypothyroidism	0 (0%)	3 (100%)	0.504
	Family history of CAD	2 (40%)	3 (60%)	0.258
	Smoking	6 (27.27%)	16 (72.73%)	0.216
	Alcohol consumption	3 (20%)	12 (80%)	0.659
	Tobacco chewing	1 (50%)	1 (50%)	0.363
PICCLE	Oedema	0 (0%)	1 (100%)	0.174
	Pallor	2 (66.67%)	1 (33.33%)	

MACE-major adverse cardiac events; SBP-systolic blood pressure; DBP-diastolic blood pressure; MI-myocardial infarction; PCI-percutaneous coronary intervention; CAD-coronary artery disease.

Table 3: Comparison of baseline clinical presentation and relevant investigations with MACE.

Parameters		MACE		p value
		Present (n=10)	Absent (n=40)	
Clinical signs and symptoms, n (%)				
Chest pain		10 (20%)	40 (80%)	-
Breathlessness		10(21.74%)	36(78.26%)	0.571
NYHA Class		0 (0%)	7 (100%)	0.002
		2 (8.33%)	22(91.67%)	
		3 (25%)	9 (75%)	
		5 (71.43%)	2 (28.57%)	
Palpitations		7 (63.64%)	4 (36.36%)	<0.001
Sweating		9 (30%)	21 (70%)	0.031
Giddiness		2 (100%)	0 (0%)	0.037
Loss of consciousness		2 (100%)	0 (0%)	0.037
Associated symptoms		1 (100%)	0 (0%)	0.200
Killip class		1 (4.35%)	22 (5.65%)	0.001
		3 (16.67%)	15(83.33%)	
		5(62.50%)	3(37.50%)	
		1 (100%)	0 (0%)	
ECG Diagnosis, n (%)	AWMI	4 (18.18%)	18(81.82%)	-
	Evolved AWMI	1 (100%)	0 (0%)	-
	IWMI	3 (37.50%)	5 (62.50%)	0.048
	IWMI, PWMI	1 (50%)	1 (50%)	-
NSTEMI		0 (0%)	12 (100%)	-
UA		1 (20%)	4 (80%)	-
Coronary angiogram diagnosis, n (%)	Double vessel disease	6 (31.58%)	13 (68.42%)	0.586
	LM	0 (0%)	1 (100%)	
	Single vessel disease	4 (15.38%)	22 (84.62%)	
	Triple vessel disease	0 (0%)	3 (100%)	-
	Triple vessel disease with LM	0 (0%)	1(100%)	-
	CIN	2 (4.76%)	40 (95.24%)	0.054

MACE-major adverse cardiac events; AWMI-anterior wall myocardial infarction; IWMI-inferior wall myocardial infarction; PWMI-posterior wall myocardial infarction; NSTEMI-non-ST-elevation myocardial infarction; UA-unstable angina; LM-left main coronary artery.

Table 4: Comparison of baseline biochemical markers with MACE.

Parameters	MACE		p value
	Present (n=10)	Absent (n=40)	
Cardiac enzymes, mean±SD			
Troponin I, ng/mL	0.68±2.15	1.67±2.59	0.008
CK, U/L	1152.00±1043.03	438.63±543.58	0.004
CKMB, U/L	139.60±129.22	68.10±69.39	0.030
Biochemical markers, mean±SD			
Total cholesterol, mg/dL	138.90±26.01	136.18±22.81	0.971
HDL, mg/dL	41.00±4.47	40.65±4.14	0.827
LDL, mg/dL	78.40±17.94	80.63±21.23	0.839
Triglycerides,mg/dL	131.40±32.72	130.65±88.39	0.409
Total bilirubin, mg/dL	1.86±1.85	0.86±0.40	0.331
AST, U/L	180.00±168.75	83.13±128.97	0.382
ALT, U/L	69.80±33.41	44.93±37.65	0.037
Sr. Sodium, meq/L	137.20±5.03	139.23±8.88	0.591
Sr. Potassium, meq/L	3.65±0.53	3.88±0.63	0.254
Urea, mg/Dl	40.00±13.82	34.23±10.22	0.409
Sr. creatinine, mg/dL	1.30±0.41	1.11±0.36	0.198
WBC count, per cumm	17580.00±7176.94	10362.50±4892.89	0.001
Neutrophils, %	78.56±5.00	69.08±9.17	<0.001
Neutrophils, per cumm	13983.43±6273.90	7319.05±4202.74	0.009
Lymphocytes, %	15.83±5.27	23.63±7.67	0.001
Lymphocytes, per cumm	2626.00±900.22	2268.43±739.45	0.267
Haemoglobin, g/L	10.10±2.25	11.24±2.04	0.169
RBC count, per cumm	3.37±0.46	3.84±0.73	0.020
Hematocrit, %	52.40±74.58	31.51±6.02	0.658
Platelet count, per cumm	249.80±78.65	234.03±61.63	0.566
Mean platelet volume (fL)	10.47±0.82	10.09±1.02	0.227
Red cell distribution width, %	14.80±2.06	14.43±1.07	0.896
WMR	1693.21±694.66	1028.64±467.80	0.003
PLR	109.97±60.31	114.44±47.72	0.451
NLR	5.58±2.08	3.40±1.69	0.002
Uric acid	5.54±1.51	5.64±1.05	0.641
Echocardiography EF, %	33.50±4.74	44.80±8.40	<0.001
Duration of stay, days	4.60±2.59	4.80±1.60	0.821

MACE-major adverse cardiac events; CK-creatine kinase; CKMB- creatine kinase myocardial band; HDL-high-density lipoprotein; LDL-low-density lipoprotein; AST-aspartate aminotransferase; ALT-alanine aminotransferase; WBC-white blood cell; RBC-red blood cell; WMR-WBC count to mean platelet volume ratio; PLR-platelet to lymphocyte ratio.

In patients with MACE, significant differences were noted with respect to mean respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), Troponin I, CK and creatine kinase myocardial band (CKMB), alanine aminotransferase (ALT), WBC count, neutrophils, lymphocytes, red blood cell (RBC) count, WMR, and ejection fraction. MACE was also associated with symptoms at presentation including palpitations, sweating, giddiness, loss of consciousness, higher Killip class and diagnosis of inferior wall myocardial infarction (IWMI) (Tables 2-4).

In this study significantly higher mean respiratory rate, lower SBP and DBP, were noted in patients with high WMR. Also, higher WMR was significantly associated with NYHA class 4, palpitations, and Killips class. Furthermore, raised mean total bilirubin, ALT levels, WBC count, neutrophils per cumm, lymphocytes, platelet count per cumm, platelet to lymphocyte ratio, uric acid and mean ejection fraction was low in patients with raised WMR (Tables 5-7).

Further, WMR with a cut-off value of 1059 was significant and highly accurate in predicting MACE with diagnostic accuracy of 72%, sensitivity of 80%, specificity of 70%, PPV of 40%, NPV of 93.33% (p=0.016) and positive likelihood ratio of 2.67 and negative likelihood ratio of 0.29 (Table 8).

Table 5: Comparison of baseline demographics and risk factors with WMR.

Parameters		WMR		p value
		High (> 1059) (n=20)	Low (≤1059) (n=30)	
Age, years (mean±SD)		62.10±13.28	55.23±11.40	0.066
Males, n (%)		13 (44.83%)	16 (55.17%)	0.312
Height, cm		171.15±8.47	167.67±7.30	0.141
Weight, kg		69.75±17.45	66.47±10.38	0.455
Body mass index, kg/m^2		23.49±4.10	23.61±3.12	0.909
Vitals, mean±SD	Pulse rate, per min	92.70±25.71	82.33±16.24	0.106
	Respiratory rate, per min	28.60±6.49	23.87±4.81	0.007
	SBP, mm Hg	111.00±20.75	127.33±21.80	0.001
	DBP, mm Hg	70.00±12.98	82.33±14.06	0.005
Risk factors, n (%)	Prior MI	1 (33.33%)	2 (66.67%)	0.651
	Prior PCI	1 (50%)	1 (50%)	0.645
	History of diabetes mellitus	8 (34.78%)	15 (65.22%)	0.487
	History of hypertension	5 (29.41%)	12 (70.59%)	0.273
	History of CKD	0 (0 %)	1 (100%)	0.600
	History of hypothyroidism	0 (0%)	3 (100%)	0.207
	Family history of CAD	2 (40%)	3 (60%)	0.690
	Smoking	10 (45.45%)	12 (54.55%)	0.485
	Alcohol consumption	7 (46.67%)	8 (53.33%)	0.529
	Tobacco chewing	2 (100%)	0 (0%)	0.155
PICCLE	Oedema	0 (0%)	1 (100%)	0.058
	Pallor	3 (100%)	0 (0%)	

WMR-WBC count to mean platelet volume ratio; SBP-systolic blood pressure; DBP-diastolic blood pressure; MI-myocardial infarction; PCI-percutaneous coronary intervention; CAD-coronary artery disease.

Table 6: Comparison of baseline clinical presentation and relevant investigations with WMR.

Parameters		WMR		p value
		High (> 1059) (n=20)	High (> 1059) (n=20)	
Clinical signs and symptoms, n (%)	Chest pain	20 (40%)	60 (60%)	-
	Breathlessness	20 (43.48%)	26 (56.52%)	0.073
NYHA class	1	0 (0.00%)	7 (100%)	0.049
	2	10 (41.67%)	14 (58.33%)	
	3	5 (41.67%)	7 (58.33%)	
	4	5 (71.43%)	2 (28.57%)	
Palpitations		8 (72.73%)	3 (27.27%)	0.016
Sweating		15 (50%)	15 (50%)	0.077
Giddiness		1 (50%)	1 (50%)	0.645
Loss of consciousness		1 (50%)	1 (50%)	0.645
Associated symptoms		1 (100%)	0 (0%)	0.400
Killip class	1	4 (17.39%)	19 (82.61%)	0.001
	2	8 (44.44%)	10 (55.56%)	
	3	7 (87.50%)	1 (12.50%)	
	4	1 (100%)	0 (0%)	
ECG Diagnosis, n (%)	AWMI	6 (27.27%)	16 (72.73%)	0.058
	Evolved AWMI	1(100%)	0 (0%)	
	IWMI	3 (37.50%)	5 (62.50%)	
	IWMI, PWMI	1 (50%)	1 (50%)	
	NSTEMI	0 (0%)	12 (100%)	
	UA	1 (20%)	4 (80%)	
Coronary Angiogram Diagnosis, n (%)	Double vessel disease	8 (42.11%)	11(57.89%)	0.901
	LM	0 (0%)	1 (100%	
	Single vessel disease	10 (38.46%)	16 (61.54%)	
	Triple vessel disease	1 (33.33%)	2 (66.67%)	-
	Triple vessel disease with LM	1 (100%)	0 (0%)	-
	CIN	18 (37.50%)	30 (62.5%)	0.155

WMR-WBC count to mean platelet volume ratio; AWMI-anterior wall myocardial infarction; IWMI-inferior wall myocardial infarction; PWMI-posterior wall myocardial infarction; NSTEMI-non-ST-elevation myocardial infarction; UA-unstable angina; LM-left main coronary artery.

Table 7: Comparison of baseline biochemical markers with WMR.

Parameters		WMR		p value
		High (>1059) (n=20)	High (>1059) (n=20)	
Cardiac enzymes, mean±SD	Troponin I, ng/mL	6.84±5.01	4.35±4.29	0.109
	CK, U/L	827.45±1016.66	417.20±358.55	0.298
	CKMB, U/L	111.30±117.16	63.13±55.80	0.156
Biochemical markers, mean±SD	Total cholesterol, mg/dL	138.80±22.65	135.33±23.89	0.427
	HDL, mg/dL	40.50±3.36	40.87±4.67	0.681
	LDL, mg/dL	79.55±19.10	80.60±21.63	0.992
	Triglycerides,mg/dL	119.60±27.70	138.27±100.95	0.421
	Total bilirubin, mg/dL	1.14±0.84	0.83±.0.44	0.046
	AST, U/L	131.65±142.66	83.07±139.59	0.048
	ALT, U/L	57.45±29.29	44.87±42.37	0.033
	Sr. Sodium, meq/L	137.45±3.95	139.73±10.13	0.517
	Sr. Potassium, meq/L	3.86±0.48	3.82±0.70	0.156
	Urea, mg/Dl	38.50±14.38	33.30±7.89	0.244
	Sr. creatinine, mg/dL	1.21±0.46	1.11±0.31	0.277
	WBC count, per cumm	17160.00±6401.02	8236.67±1660.80	<0.001
	Neutrophils, %	75.89±7.89	67.70±8.78	0.100
	Neutrophils, per cumm	13232.52±5799.54	5598.20±1438.07	0.048
	Lymphocytes, %	16.89±4.92	25.52±7.60	0.033
	Lymphocytes, per cumm	2730.90±749.20	2079.30±691.86	0.517
	Haemoglobin, g/L	10.40±2.40	11.42±1.82	0.244
	RBC count, per cumm	3.51±0.61	3.92±0.74	0.277
	Hematocrit, %	29.61±5.63	31.82±6.24	0.166
	Platelet count, per cumm	261.90±60.21	220.70±63.40	0.025
	Mean platelet volume (fL)	10.10±0.79	10.21±1.12	0.681
	Red cell distribution width, %	14.52±1.72	14.49±0.99	0.937
	PLR	105.09±44.94	119.17±52.83	0.259
	NLR	4.99±1.95	3.06±1.56	<0.001
	Uric acid	6.02±0.98	5.36±1.18	<0.001
	Echocardiography EF, %	37.10±6.51	46.17±8.68	<0.001
	Duration of stay, days	4.35±1.79	5.03±1.81	0.301

WMR-WBC count to mean platelet volume ratio; CK-creatine kinase; CKMB- creatine kinase myocardial band; HDL-high-density lipoprotein; LDL-low-density lipoprotein; AST-aspartate aminotransferase; ALT-alanine aminotransferase; WBC-white blood cell; RBC-red blood cell; WMR-white blood cell count to mean platelet volume ratio; PLR-platelet to lymphocyte ratio, NLR-neutrophil to lymphocyte ratio.

Table 8: Accuracy of WMR in predicting MACE.

WMR	MACE		
	Yes	No	Total
	n (%)	n (%)	n (%)
High (>1059)	8 (80%)	12 (30%)	20 (40%)
Low (≤1059)	2 (20%)	28 (70%)	30 (60%)
Total	10 (20%)	40 (80%)	50 (100%)

WMR- WBC count to mean platelet volume ratio; MACE- major adverse cardiac events; sensitivity=80%; specificity=70%; positive predictive value=40%; negative predictive vale=93.33%; p=0.016; diagnostic accuracy=72%; positive likelihood ratio =2.67; negative likelihood ratio=0.29

DISCUSSION

The present study demonstrates that, raised WMR is a novel non-invasive marker which is highly accurate in predicting MACE in patients presenting with ACS. Raised WMR that is, with a cut-off value of 1059 with AUC of 0.825 (SE=0.074; 95% CI: 0.679-0.971; p=0.001) was significant and highly accurate in predicting MACE with higher diagnostic accuracy (72%), sensitivity (80%), specificity

(70%) and low PPV (40%) but high NPV (93.33%) and high positive likelihood ratio (2.67) and lower negative likelihood ratio (0.29) (p=0.016).

Apart from WMR, higher respiratory rate, CK and CKMB, ALT, WBC count, neutrophils, neutrophil to lymphocyte ratio (NLR), lower SBP, DSP, Troponin I, lymphocytes, RBC count, and ejection fraction were other predictors of MACE. Also, symptoms including palpitations, sweating, giddiness, loss of consciousness, higher Killip class, and diagnosis of IWMI at admission were independent predictors of MACE.

Furthermore, higher respiratory rate, mean total bilirubin, AST, ALT levels, WBC count, neutrophils, lymphocytes, NLR, uric acid, lower SBP, DBP, and ejection fraction were the independent predictors of raised WMR. Also, higher WMR was significantly associated with NYHA class 4, palpitations, Killip's class 4.

Although, WMR is a ratio derived from WBC count to MPV ratio, surprisingly the present study illustrated that baseline MPV level is not a predictor of MACE as mean MPV levels in patients with MACE (10.47±0.82 fL) and without MACE (10.09±1.02 fL) were statistically comparable (p=0.227). This is similar to a study by Dehgani MR et al, which found no relationship between elevated baseline MPV and prognosis and incidence of MACE in ACS patients.[9] The observation of the present study was also partly in agreement with a recent study by Adam AM et al, who in their study illustrated that admission MPV level is not a predictor of cardiovascular events at 30 days of follow-up.[10] In contrast, a study by Estévez-Loureiro et al, found that raised MPV is an independent predictor of 30-day mortality in patients with STEMI undergoing primary PCI.[15] Vagdatli et al, stated that platelet distribution width (PDW), a measure of variability in platelet size, is a more specific marker of platelet activation than MPV.[16] Therefore, MPV may not be used in the clinical setting for short-term outcomes due to its lesser specificity and discriminative ability as compared to other complete blood count (CBC) components. MPV is a potentially useful platelet activation marker which is a widely available and easily measured hematologic parameter in a CBC test. There has been a wide array of results in previous literature, with some studies proving admission MPV to be a useful prognostic tool, in patients with ACS, while others completely disproving it.[15,17,18]

In the present study, on the contrary to mean MPV, mean WBC count was found to be significantly high in patients with MACE (17580.00±7176.94/cumm) compared to those who did not develop MACE (10362.50±4892.89/cumm) and the difference was profound (p<0.001). An increased leukocyte count is a prominent indicator of compromised microvascular reperfusion. Prior ACS studies have demonstrated the use of NLR as an admission prognostic marker and a risk stratification tool of adverse outcomes, albeit there have been conflicting results in terms of the most appropriate leukocyte subtype. [6,19-23] He J et al, reported that average NLR was a useful and powerful predictor of mortality and in-hospital cardiovascular events in Chinese patients presenting with STEMI, thus providing additive predictive value to conventional risk factors and commonly used biomarkers e.g. C-reactive protein (CRP).[24] Similarly, Barron HV et al, presented that acute MI patients with a leukocyte count in the highest quintile had a higher 30-day mortality rate than patients with a leukocyte count in the lower quintiles.[25] In this study, it was also found that WBC count was associated with MACE an observation partly in agreement with the studies by He J et al, and Barron HV et al.[24,25]

The present study demonstrated that raised WMR that is, with a cut-off value of 1059 holds greater predictive value for short-term MACE in patients presenting with ACS yielding higher diagnostic accuracy (72%), sensitivity (80%), specificity (70%) with low PPV (40%) and high NPV (93.33%) as well as high positive likelihood ratio (2.67) and lower negative likelihood ratio (0.29) (p=0.016). Recently Adam AM et al, reported sensitivity of 68.3% and specificity of 63.7% with a slightly higher WMR cut-off values (1068.75, AUC=0.734 95% CI: 0.656-0.812; p<0.001) which is very much comparable with the present study although there was slightly higher cut-off value in the study by Adam AM et al, compared to the present study (1068.75 vs 1059) which can be explained by the methodological differences in the two studies viz. the study by Adam AM et al, was comprised of large sample size compared to the present study (n=297 vs n=50) and the study by Adam AM et al, evaluated not only WMR in combination with cardiac enzymes.[10] Also the study by Adam AM et al, had higher rate of MACE (34.34% compared to 10% in the present study).[10]

It is speculated that, WMR incorporates two of the most prominent inflammatory mediators, namely MPV and WBC count, into a single value. MPV is a measure of platelet size, and larger platelets are known to be enzymatically more active and have a greater thrombotic potential and are thus more likely to occlude the coronary vessels. Whereas leukocytes may cause oxidative and proteolytic damage, induce hypercoagulability and activate tissue factor. These mechanisms may lead to thrombus formation and infarct expansion.[10] These findings are consistent with the studies conducted by Dehghani MR et al, who found that WMR is a better predictor of long-term mortality and incidence of adverse outcomes in patients with NSTEMI than WBC and MPV.[8,9] A similar analysis performed by Çiçek G et al, showed the superiority of elevated WMR levels on admission, in predicting long-term mortality and MACE incidence in STEMI patients as compared to other CBC components, such as MPV, red blood cell distribution width (RDW), PLR-NLR and WBC-MPV combinations.[26] Results show that WMR had a higher sensitivity to predict short-term outcomes therefore,

calculating WMR is not only sensitive but a faster and a more efficient marker.

Overall, the present study demonstrates that, raised WMR (≥1059) is highly accurate in discriminating the poor outcome that is MACE within 30 days in patients presenting with ACS. Furthermore, ACS patients with raised WMR along with higher respiratory rate, CK and CKMB, ALT, WBC count, neutrophils, NLR, total bilirubin, AST, ALT levels, WBC count, lymphocytes, uric acid and lower SBP, DBP, troponin I, RBC count, and ejection fraction as well as the symptoms at presentation that is, palpitations, sweating, giddiness, loss of consciousness, higher Killip class, and diagnosis of IWMI are at significantly higher risk of 30 days MACE events and prompt not only meticulous follow up but early diagnosis and management of MACE events within 30 days in order to avoid future consequences leading to morbidity and mortality. However, these conclusions require careful interpretation due to potential limitations of this study viz. the conclusions drawn from the present study were based on a single-centre study comprised of relatively smaller sample size using a non-randomized sampling technique. Which limits the generalizability of the study to the entire population. Secondly, we conducted CBC once rather than serial testing at regular time-intervals. Furthermore, we did not measure other, more specific pro-inflammatory markers including P-selectin, high-sensitivity CRP, interleukins, selectin molecules, adhesion ligands and receptors, and markers of oxidative stress to show any comparison between WMR and such biomarkers. Further studies are required to validate these results and define the exact role of WMR in predicting short-term MACE.

CONCLUSION

Higher WMR value is an easily accessible and an inexpensive indicator on admission associated with worse short-term outcomes in patients with ACS and independently predict the short-term MACE. Furthermore, the risk of short-term (30 days) MACE increases with higher respiratory rate at presentation, CK and CKMB, ALT, WBC count, neutrophils, NLR, total bilirubin, AST, lymphocytes, uric acid, lower SBP, DBP, Troponin I, RBC count, and ejection fraction as well as the symptoms at presenting that is, palpitations, sweating, giddiness, loss of consciousness, higher Killip class, and diagnosis of IWMI.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Gupta R, Joshi P, Mohan V, Reddy K, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart. 2008;94(1):16-26.
2. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet. 1997;349(9061):1269-76.
3. Reddy KS. Cardiovascular diseases in India. World health statistics quarterly Rapport trimestriel de statistiques sanitaires mondiales 1993;46(2):101-7.
4. Nayak MT, Kamath V. Outcome of endoscopic third ventriculostomy: Analysis of first 23 cases. Inter J Adv Med. 2002;2(2):94-9.
5. Libby P. Mechanisms of acute coronary syndromes and their implications for therapy. N Engl J Med. 2013;368:2004-13.
6. Dehghani MR, Rezaei Y, Taghipour-Sani L. Superiority of total white blood cell count over other leukocyte differentials for predicting long-term outcomes in patients with non-ST elevation acute coronary syndrome. Biomarkers. 2014;19(5):378-84.
7. Rechciński T, Jasińska A, Foryś J, Krzemińska-Pakuła M, Wierzbowska-Drabik K, Plewka M, et al. Prognostic value of platelet indices after acute myocardial infarction treated with primary percutaneous coronary intervention. Cardiol J 2013;20(5):491-8.
8. Dehghani MR, Rezaei Y, Fakour S, Arjmand N. White blood cell count to mean platelet volume ratio is a prognostic factor in patients with non-ST elevation acute coronary syndrome with or without metabolic syndrome. Korean Circ J 2016;46(2):229-38.
9. Dehghani MR, Rezaei Y, Taghipour-Sani L. White blood cell count to mean platelet volume ratio as a novel non-invasive marker predicting long-term outcomes in patients with non-ST elevation acute coronary syndrome. Cardiol. J 2015;22(4):437-45.
10. Adam AM, Rizvi AH, Haq A, Naseem R, Rehan A, Shaikh AT, et al. Prognostic value of blood count parameters in patients with acute coronary syndrome. Indian Heart J. 2018;70(2):233-40.
11. Mello BHGd, Oliveira GBF, Ramos RF, Lopes BBC, Barros CBS, Carvalho EdO, et al. Validation of the Killip-Kimball classification and late mortality after acute myocardial infarction. Arq Bras Cardiol. 2014;103(2):107-17.
12. Raphael C, Briscoe C, Davies J, Whinnett ZI, Manisty C, Sutton R, et al. Limitations of the New York Heart Association functional classification system and self-reported walking distances in chronic heart failure. Heart. 2007;93(4):476-82.
13. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. Eur Heart J. 2007;28(20):2525-38.
14. Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. Harrison's principles of internal medicine: McGraw-Hill Companies; 2015.
15. Estévez-Loureiro R, Salgado-Fernández J, Marzoa-Rivas R, Barge-Caballero E, Pérez-Pérez A, Noriega-Concepción V, et al. Mean platelet volume predicts patency of the infarct-related artery before mechanical reperfusion and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous

coronary intervention. Thromb Res. 2009;124(5):536-40.
16. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia. 2010;14(1):28-32.
17. Goncalves SC, Labinaz M, Le May M, Glover C, Froeschl M, Marquis JF, et al. Usefulness of mean platelet volume as a biomarker for long-term outcomes after percutaneous coronary intervention. Am J Cardiol. 2011;107(2):204-9.
18. Shah B, Oberweis B, Tummala L, Amoroso NS, Lobach I, Sedlis SP, et al. Mean platelet volume and long-term mortality in patients undergoing percutaneous coronary intervention. Am J Cardiol. 2013;111(2):185-9.
19. D'Ascenzo F, Biondi-Zoccai G, Moretti C, Bollati M, Omedè P, Sciuto F, et al. TIMI, GRACE and alternative risk scores in Acute Coronary Syndromes: a meta-analysis of 40 derivation studies on 216,552 patients and of 42 validation studies on 31,625 patients. Contemp Clin Trials. 2012;33(3):507-14.
20. Brkovic V, Dobric M, Beleslin B, Giga V, Vukcevic V, Stojkovic S, et al. Additive prognostic value of the SYNTAX score over GRACE, TIMI, ZWOLLE, CADILLAC and PAMI risk scores in patients with acute ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention. Int J Cardiovasc Imaging. 2013;29(6):1215-28.
21. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol. 2005;45(10):1638-43.
22. Sabatine MS, Morrow DA, Cannon CP, Murphy SA, Demopoulos LA, DiBattiste PM, et al. Relationship between baseline white blood cell count and degree of coronary artery disease and mortality in patients with acute coronary syndromes: A TACTICS-TIMI 18 substudy. J Am Coll Cardiol. 2002;40(10):1761-8.
23. Huang G, Zhong X, Zhong B, Chen Y, Liu Z, Su L, et al. Significance of white blood cell count and its subtypes in patients with acute coronary syndrome. Eur J Clin Invest. 2009;39(5):348-58.
24. He J, Li J, Wang Y, Hao P, Hua Q. Neutrophil-to-lymphocyte ratio (NLR) predicts mortality and adverse-outcomes after ST-segment elevation myocardial infarction in Chinese people. Int J Clin Exp Pathol. 2014;7(7):4045.
25. Barron HV, Harr SD, Radford MJ, Wang Y, Krumholz HM. The association between white blood cell count and acute myocardial infarction mortality in patients≥ 65 years of age: findings from the cooperative cardiovascular project. J Am Coll Cardiol. 2001;38(6):1654-61.
26. Cicek G, Acikgoz SK, Yayla C, Kundi H, Ileri M. White blood cell count to mean platelet volume ratio: A novel and promising prognostic marker for ST-segment elevation myocardial infarction. Cardiol J. 2016;23(3):225-35.

Cite this article as: Shanker S, Reddy S, Ramachandran G. Usefulness of white blood cell count to mean platelet volume ratio in predicting short term, 30 days major adverse cardiac events in patients presenting with acute coronary syndrome. Int J Res Med Sci 2020;8:1404-13.