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Original Article

The pattern of on-admission hematological cellular response in patients with ST segment elevated myocardial infarction

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Abstract

Background

According to current understanding, atherosclerosis is believed to be inflammatory in origin. Haematological parameters, as markers of inflammation, have been shown to be linked to various outcomes among patients with ST segment elevated myocardial infarction (STEMI).

Objectives

To identify the pattern of haematological cellular response in patients with STEMI and to compare the results among patients with different sub-groups of STEMIs.

Methods

A descriptive cross-sectional study was conducted at the Cardiology Unit, Teaching Hospital, Kandy in 2016 and 2017. Full blood counts of all eligible patients who had acute STEMI were obtained on admission. Patients with clinical evidence of inflammatory or infectious conditions preceding STEMI were excluded. Controls were defined as patients who had STEMI six months previously and were treated with medical thrombolysis with no further events of acute coronary syndrome. Haematological parameters of white blood cell (WBC) count, neutrophil/lymphocyte ratio (NLR), mean platelet volume (MPV), platelet distribution width (PDW), and platelet/lymphocyte ratio (PLR) were evaluated. Diabetic sub group was compared with age and sex matched non-diabetic group. Comparison also made among groups with different extensions of the anterior and inferior STEMI.

Results

There were 350 patients with acute STEMI and 250 age and sex matched controls in the study. Of the patients, 259(74.00%) were males. The mean age of the patients was 61.27±11.64 years. There was a significant higher value noted in absolute NLR (7.00±5.86 vs. 5.55±4.32, p=0.00), PDW (16.61±2.32 vs. 14.58±2.51, p=0.00) and PLR (164.42±111.21 vs. 122.79±64.46, p=0.00) in acute STEMI patients compared to controls. Out of the STEMI patients 20.86% (n=73) were diabetics. There was a significant higher value noted in NLR (9.43±6.66 vs. 6.62±7.14, p=0.00), PDW (17.62±3.31 vs. 13.61±1.52, p=0.00) and PLR (178.32±121.24 vs. 146.50±102.34) among diabetic vs. non-diabetic patients. In relation to territory of the infarct, there was a significantly higher NLR (8.88±6.32 vs. 7.21±6.12, p=0.00) and PLR (176.62±135.62 vs142.58±112.89, p=0.00) in the anterior STEMI group compared to the inferior STEMI patients.

Conclusion

Leucocytes, platelets and their cell distribution characteristics have their own unique patterns of behaviour in patients with acute STEMI. These observations need further elaboration with respect to cell biology and cytochemical aspects, since they may have the potential to predict plaque instability and determine prognosis.

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Introduction

Ischaemic heart disease is still the leading cause of death worldwide [0] and has a prevalence of 9.3% in Sri Lanka [2]. Although the disease is highly prevalent, elucidation of its pathogenesis is still ongoing due to the complexity of the disease. It is interesting to note that, even in the current era, novel contributing factors to the aetio-pathology of coronary artery disease (CAD) are being added to the traditional vascular risk factors. Evidence is mounting that CAD is a result of generalized inflammation that results in promotion of atherosclerosis [3]. However, the precise mechanism and the contribution of generalized inflammation to the pathophysiology of CAD remains uncertain.

Several recent studies have addressed the role of chemokines in leukocyte accumulation in atherosclerosis and extended our knowledge and understanding of the complex cell types involved in vascular injury [4]. In addition, some clinical studies have shown that several cellular biomarkers are able to predict future ischaemic events and adverse cardiac outcomes following acute coronary syndromes [3]. Therefore, inclusion of the pattern of the initial haematological response as a prognostic marker in STEMI to current risk scores has become an area of emerging research interest in clinical cardiology.

Objectives

The main objective of the study was to describe the pattern of the on-admission haematological cellular response in patients with STEMI and to compare this among patients with different sub-groups of STEMI.

Material and methods

Study design: A descriptive cross-sectional study was conducted at the Cardiology Unit, Teaching Hospital, Kandy, from November 2016 to December 2017, on consecutive patients admitted with STEMI. FBC findings were compared with age and sex matched controls consecutively collected during the same period. The control group consisted of patients who had uncomplicated STEMI 6 months previously with no further acute coronary events.

Inclusion criteria: A diagnosis of STEMI was defined as the occurrence of classic symptoms of coronary ischaemia within 12 hours of admission, elevation of cardiac biomarkers and detection of ST-segment elevation in two contiguous leads, as stated in the guidelines of the American College of Cardiology and the European Society of Cardiology [5,6].

Exclusion criteria: Patients having clinical evidence of ongoing active infection, systemic inflammatory disease, known hematological disease, end-stage liver and kidney disease, known systemic autoimmune disease, known malignancy, presence of left bundle branch block, paced ventricular rhythm on the presenting ECG and patients with inadequate laboratory data were excluded. Patients with STEMI who presented 12 hours or more after initial symptoms were also excluded from the study.

Haematological and Biochemical analysis: Blood samples were drawn from the antecubital vein on admission. Cell parameters were analyzed using a single automated FBC analyzer. Haematological parameters of white blood cell (WBC) count,

neutrophil/lymphocyte ratio (NLR), mean platelet volume (MPV), platelet distribution width (PDW), and platelet/lymphocyte ratio (PLR) were determined for each patient.

Electrocardiographic analysis: 12 lead ECG was obtained immediately after admission at 25mm/sec paper speed, and 10 mV gain. STEMI was determined by the occurrence of ST segment elevation of 0.2 mV in males and 0.15mV in females measured at the J point in leads V_2-V_3 or 0.1 mV on at least two contiguous leads of the remaining leads.

Demographic and clinical data: Demographic details and clinical data, including co-morbidities and other vascular risk factors were obtained.

Statistical analysis: Continuous variables were presented as mean with standard deviation (SD) and categorical variables as percentages. Independent sample *t test* was used to compare quantitative data, between the groups. Differences were considered statistically significant when the *p* value was <0.05. The Statistical Package for Social Sciences version 17 was used for all calculations and statistical analyses.

Ethics clearance: Ethics clearance was obtained from the Ethical and Research Committee of Teaching Hospital, Kandy. Informed written consent was obtained from the all patients

Results

Demographic data

There were 350 patients with acute STEMI and 250 age and sex matched controls in the study. Baseline characteristics and co-morbidities of the patients and controls are given in Table 01.

Table 01: Baseline characteristics of the patients with acute STEMI and Control group

Variable	**Acute STEMI**	**Controls**
Age (years) **(mean ± SD)**	61.27± 11.64	59.80±11.90
Gender		
Male	259 (74.00%)	178(71.20%)
Female	91 (26.00%)	72(28.80%)
Co-morbidities		
Diabetes Hypertension Dyslipidemia	73 (20.86%) 45 (12.86%) 82 (23.43%)	32 (12.80%) 18 (07.20%) 36 (14.40%)
*SD = Standard deviation		

In the STEMI group, 44.00% (n=154) and 56.00% (n=196) had anterior and inferior territory involvement, respectively.

Haematological response of acute STEMI patients versus controls

There was a significantly higher value noted in absolute NLR (7.00±5.86 vs. 5.55±4.32, p<0.001), PDW (16.61±2.32 vs. 14.58±2.51, p<0.001) and PLR (164.42±111.21 vs. 122.79±64.46, p<0.001) in acute STEMI patients compared to controls. Though a higher WBC count was seen in acute STEMI patients (13.23±4.62 vs. 11.61±4.82, p=0.26) it was not statistically significant (Table 02).

Table 02: Comparison of haematological parameters of acute STEMI patients and controls

Parameter	Acute STEMI (n=350) *Mean ± SD*	Controls (n=250) Mean ± SD	P value
WBC	13.23±4.62	11.61±4.82	0.26
NLR	7.00±5.86	5.55±4.32	0.00
MC	0.81±0.85	0.81±1.12	0.45
WBC/MPV	1.42±0.51	1.43±0.59	0.22
HB	13.21±3.54	13.32±3.42	0.15
RDW	13.30±3.31	13.44±2.86	0.88
RDW/PLT	0.10±0.00	0.10±0.00	0.46
MPV	8.87±1.01	7.75±0.90	0.00
PDW	16.61±2.32	14.58±2.51	0.00
PLR	164.42±111.2	122.79±64.4	0.00

STEMI=ST segment elevated myocardial infarction WBC=Total White Blood cell count ($\times 10^9$/µL), NLR=Neutrophil-to-lymphocyte ratio, MC=Monocyte Count ($\times 10^9$/µL), WBC/MPV=Total white blood cell count to Mean Platelet Volume ratio, HB=Haemoglobin level (g/dL), RDW=Red blood cell distribution width (%), RDW/PLT=Red blood cell distribution width to Platelet count ratio, MPV=Mean Platelet Volume (fL), PDW=Platelet Distribution width, PLR=Platelet to lymphocyte ratio

Haematological response of acute STEMI patients with who had diabetes versus non-diabetics

Of the STEMI patients, 20.86% (73/350) were diabetics. There was a significant higher value noted in NLR (9.43±6.66 vs. 6.62±7.14, p<0.001), PDW (17.62±3.31 vs. 13.61±1.52, p<0.001) and PLR (178.32±121.24 vs. 146.50±102.34, p<0.001) among diabetic than non-diabetic patients (Table 03).

Table 03: Comparison of haematological parameters of acute STEMI patients with and without diabetes

Parameter	Diabetics(n=73) *Mean ± SD*	non-Diabetics(n=277) *Mean ± SD*	*P Value*
WBC	13.18±4.04	13.10±4.71	0.75
NLR	9.43±6.66	6.62±7.14	0.00
MC	0.87±0.23	0.84±0.75	0.86
WBC/MPV	1.45±0.48	1.47±0.62	0.43
HB	12.86±1.53	14.92±3.87	0.36
RDW	6.93±2.31	8.55±2.33	0.56
RDW/PLT	0.10±0.02	0.10±0.02	0.92
MPV	8.93±0.81	8.65±0.68	0.78
PDW	17.62±3.31	13.61±1.52	0.00
PLR	178.32±121.24	146.50±102.34	0.00

STEMI=ST segment elevated myocardial infarction WBC=Total White Blood cell count ($\times 10^9$/μL), NLR=Neutrophil-to-lymphocyte ratio, MC=Monocyte Count ($\times 10^9$/μL), WBC/MPV=Total white blood cell count to Mean Platelet Volume ratio, HB=Haemoglobin level (g/dL), RDW=Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV=Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR=Platelet to lymphocyte ratio

Haematological response of acute STEMI patients with respect to territory and extension

Anterior STEMI comprised 44.00% (154/350) of patients. Out of them, 24.03% (n=37) had antero-septal STEMI (V_1-V_3 extension) and 75.97% (n=117) had anterior STEMI extending beyond V_1-V_3 territory. Inferior STEMI comprised 56.00% (196/350), with 77.55% (n=152) confined to the inferior territory and 22.45% (n=44) extending to the posterior and right ventricular territory.

Table 04: Comparison of the haematological parameters of acute STEMI patients with respect to anterior and inferior involvement

Parameter	Anterior STEMI (n=154) *Mean ± SD*	Inferior STEMI(n=152) *Mean ± SD*	P Value
WBC	14.31±3.22	11.45±4.56	0.35
NLR	8.88±6.32	7.21±6.12	0.00
MC	0.82±0.81	0.83±1.11	0.64
WBC/MPV	1.67±0.44	1.43±0.65	0.67
HB	12.35±2.54	13.52±3.11	0.23
RDW	7.29±2.95	13.45±1.93	0.46
RDW/PLT	0.10±0.01	0.10±0.02	0.95
MPV	8.78±0.81	8.65±0.73	0.68
PDW	16.62±2.34	15.23±2.51	0.45
PLR	176.62±135.62	142.58±112.89	0.00

STEMI=ST segment elevated myocardial infarction, WBC=Total White Blood cell count ($\times 10^9$/μL), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9$/μL), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, HB=hemoglobin level (g/dL), RDW=Red blood cell distribution width (%), RDW/PLT=Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR=Platelet to lymphocyte ratio

There was a significantly higher NLR noted in the anterior STEMI group (8.88±6.32) vs the inferior STEMI group (7.21±6.12, p=0.00) and a significantly higher PLR in anterior STEMI (176.62±135.62) group than inferior STEMI group (142.58±112.89) (p=0.00) (Table 04).

In the anterior STEMI group, there was a significantly higher NLR noted in the subgroup with anterior STEMI extending beyond the V1-V3 territory (8.85±6.53) vs antero-septal STEMI (V1-V3) (7.12±5.46) (p=0.00). However, in the inferior STEMI group there was no significant difference of cellular parameters between patients with STEMI confined to the inferior territory vs those with extension (Table 05).

Table 05: Comparison of haematological parameters of acute STEMI patients related to extension of STEMI [Antero Septal (V_1-V_3) versus STEMI beyond V_1-V_3]

Anterior STEMI			
Parameter	**Antero Septal (V_1-V_3) (n=37)** ***Mean ± SD***	**STEMI beyond V_1-V_3 (n=117)** ***Mean ± SD***	**P value**
WBC	13.37±0.53	13.45±1.03	0.06
NLR	7.12±5.46	8.85±6.53	0.00
MC	0.79±0.75	0.81±0.92	0.63
WBC/MPV	1.66±0.32	1.64±0.45	0.56
HB	14.35±1.36	14.12±2.32	0.02
RDW	8.21±1.95	9.45±1.23	0.79
RDW/PLT	0.10±0.00	0.10±0.01	0.16
MPV	8.45±0.25	8.82±0.63	0.34
PDW	15.53±2.22	16.25±1.96	0.48
PLR	165.85±95.63	156.34±101.56	0.33
Inferior STEMI			
Parameter	**Confined Inferior STEMI (n=152)** ***Mean ± SD***	**Extended Inferior STEMI (n=44)** ***Mean ± SD***	**P value**
WBC	13.36±2.56	13.89±3.52	0.50
NLR	7.56±5.62	8.08±4.56	0.35
MC	0.79±0.22	0.81±0.96	0.75
WBC/MPV	1.52±0.13	1.51±0.25	0.08
HB	13.56±1.26	13.25±2.35	0.85
RDW	8.56±1.98	10.26±1.85	0.19
RDW/PLT	0.10±0.01	0.10±0.02	0.23
MPV	8.78±0.45	7.96±0.62	0.56
PDW	15.95±1.95	15.65±1.96	0.82
PLR	156.32±99.62	143.45±86.32	0.33

STEMI=ST segment elevated myocardial infarction WBC=Total White Blood cell count ($\times 10^9/\mu L$), NLR= Neutrophil-to-lymphocyte ratio, MC= Monocyte Count ($\times 10^9/\mu L$), WBC/MPV= Total white blood cell count to Mean Platelet Volume ratio, HB=hemoglobin level (g/dL), RDW=Red blood cell distribution width (%), RDW/PLT= Red blood cell distribution width to Platelet count ratio, MPV= Mean Platelet Volume (fL), PDW= Platelet Distribution width, PLR= Platelet to lymphocyte ratio

Discussion

The growth and propagation of an atherosclerotic plaque is a complex cardiac disorder involving both acute and chronic inflammatory processes. Traditional vascular risk factors, such as hypertension, diabetes, gender and genetic factors, add to the evolution of coronary plaque disease. However, a vital role is played by inflammatory cells in this complicated process [7,8,9].

During the course of formation of a coronary plaque, endothelial damage occurs which dis-regulates vasomotion and increases permeability of the endothelium. Aggregation of platelets, leukocyte adhesion and cytokine generation promotes atherosclerosis [10]. The role of pro-inflammatory cytokines in atheromatous plaque rupture is also well-established [11]. The association of altered leukocyte counts in blood with an augmented risk for ischaemic cardiac events and mortality in patients with acute coronary syndromes has been borne out by many studies [12].

In our study, although leucocytosis is noted in the acute STEMI group, only the NLR is significantly increased compared to the control group. This may reflect the complex cell types and finer cytochemical mediation involved in atheromatous plaque rupture. This finding is strengthened by studies indicating that the NLR has a strong link to the plasma atherogenic index [13] Further studies are needed to identify the changes in neutrophil and lymphocyte concentrations that predict ACS in a high-risk patient.

Another interesting finding in our study is the association between PDW and PLR and acute STEMI. This association has been previously described by Varasteh-ravan *et al*. in Iran [14]. This may reflect initial haematological changes in respect to platelets occurring in the peri-infarction period. A higher PDW may be related to acute or sub-acute alterations of platelet morphology that happen during this period. The alteration in the proportion of platelets and lymphocytes may also reflect inter-cellular interactions induced by generalized inflammation, which are related to acute atheromatous plaque rupture. Therefore, further research is required to identify the precise cytochemical signals that occur in this period for further elucidation of these phenomena.

In the diabetic population, CAD is a major cause of morbidity and mortality. Several prospective studies have shown that higher levels of pro-inflammatory markers or depleted levels of anti-inflammatory markers predict the development of diabetes [14,15,16,17,18]. Therefore, there may be a link between the increased vascular inflammation seen in diabetics and the higher risk of CAD. The significantly higher value of NLR, PDW and PLR in diabetics with STEMIs vs non-diabetics with STEMI may reflect that diabetic patients may have a higher vascular inflammatory response compared to non-diabetics.

High values of NLR and PLR in diabetic patients have been described by Akbas *et al*. and this was postulated to result from increased inflammation and endothelial dysfunction in this population [19]. Other studies have shown that white cell counts appear to be an independent predictor of the severity of CAD in diabetics [20]. The interaction of

leucocytes and platelet cell signaling in relation to the timing of atheromatous plaque rupture in diabetic patients is worth exploring.

The observation, in our study, that higher NLR and PLR occurs in anterior STEMI compared to inferior STEMI may be related to the larger infarcted area seen in anterior vs inferior STEMIs. This is supported by that fact that the NLR is higher among the subgroup with extensive anterior STEMI. It is not clear why this is not observed in the inferior STEMI group.

A limitation of our observational study design is that it is difficult to determine whether these FBC parameters are a cause or result of atheromatous plaque rupture. In addition, the STEMI group and the control group were not matched with regard to co-morbidities such as diabetes.

Conclusion

Leucocytes, platelets and their cell distribution have a characteristic pattern of behavior in acute STEMI and varies with the presence or absence of diabetes and with the site and extension of the infarction. These observations need further elaboration in relation to the underlying cell biology and cytochemical aspects, with a view to using these parameters to determine the timing of plaque instability. Further large-scale prospective studies are needed to elucidate the precise role of these FBC parameters in forecasting short-term and long-term prognosis in patients with CAD.

Limitations

The study was conducted at one of the major cardiology centres in Sri Lanka. However, expanding the study to a multicenter study would have given a more representative sample of the whole population.

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