Association of White Blood Cell Count and Severity of Lesion in Coronary Artery Disease in the Setting of Acute Coronary Syndrome

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ABSTRACT

BACKGROUND

The present study was designed to determine the relationship between the white blood cell (WBC) count, clinical outcomes, severity of coronary artery lesion and angiographic characteristics in patients with acute coronary syndrome (ACS).

METHODS

This is a single-center, cross-sectional study conducted at a tertiary care center in India, from March 2012 to February 2013, and included 103 ACS patients. All the patients were evaluated based on their medical history, physical and clinical examinations. Blood sample was received from each patient at admission and before discharge or after 7 days whichever was earlier to determine total WBC count.

RESULTS

The mean age of all the patients was 56.14 ± 11.04 years. A total of 82 (79.6%) patients presented with ST-segment elevation myocardial infarction and 21 (20.4%) patients presented with unstable angina / non-ST segment elevation myocardial infarction. Significant increase in WBC count was observed in patients with ejection fraction ≤40%, congestive heart failure, shock, left anterior descending coronary artery lesions, active thrombus and in dead patients.

CONCLUSIONS

The results of the present study further strengthen the links between inflammation and cardiovascular disease and support the previous finding that WBC count is a strong independent predictor of short term mortality and morbidity in ACS patients. Thus, WBC count may become an additional parameter for the preliminary approach of ACS patients.

KEYWORDS

Acute Coronary Syndrome, Cardiovascular Diseases, Inflammation, White Blood Cells

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BACKGROUND

Inflammation is one of the pathophysiological mechanisms involved in the development of atherosclerosis and acute coronary syndromes (ACS), which are considered as the most important causes of sudden cardiac death, acute myocardial infarction and unstable angina. Certain inflammatory markers such as C-reactive protein, B-type natriuretic peptide, troponin, interleukin-6, white blood cell (WBC) count and many more have been identified to be associated with increased incidence of cardiovascular complications and death in patients with ACS.[1-4] Among all the available inflammatory markers, WBC count is a simple test that is considered to be one of the most common and universally available in routine clinical practice.

The relationship between elevated WBC count and coronary heart disease is strong, consistent, and biologically plausible. The WBC count plays a crucial role in the reparative process that take place to replace the necrotic tissue for collagen in ACS. Thus, elevated WBC count typically indicate inflammation and plays a key role in the atherogenesis, atherosclerotic plaque rupture and thrombosis. Recent studies have shown that WBC destabilize coronary artery plaque at the onset of ACS, and the elevated WBC count (leucocytosis) is considered to be an independent predictor of both short and long term cardiac mortality, cardiovascular complication and adverse outcome in ACS patients and also predict future cardiovascular events, even in healthy individuals who are free of coronary artery disease.[4-6]

The study was undertaken to find out the association between WBC count, clinical outcomes and angiographic findings in patient with ACS to strengthen earlier observations. The aim of the present study was to determine the relationship between the WBC count, clinical outcomes, severity of coronary artery lesion and other angiographic characteristics in ACS patients.

METHODS

This was a single-center, cross-sectional study conducted at a tertiary care center in India between March, 2012 to February, 2013. The study included 103 patients who were diagnosed with ACS. The patients who died or developed mechanical complication before coronary angiography, refuse or underwent coronary angiography after 24 hours of presentation, with renal dysfunction (serum creatinine ≥2 mg/dL), hepatic disorders, inflammatory/neoplastic diseases or any systemic disorders, acute/chronic infectious disease or; on medications which can affect WBC counts were excluded from the study. The study was conducted as per standard good clinical practice guideline and declaration of Helsinki. The written informed consent was received from either patient or from patient's relatives before the conduct of the study.

All the patients were evaluated based on their medical history, physical and clinical examinations. Blood sample was obtained from each patient to determine WBC count immediately after admission and after 7 days or before discharge whichever was earlier. The WBC count was divided into three categories, Group-1 (<10000 cells/mm^3), Group-2 (10000-15000 cells/mm^3) and Group-3 (>15000 cells/mm^3). Echocardiography was performed during admission and before discharge, especially to determine regional wall motion abnormality, ejection fraction, chamber dimensions and other complications. Coronary angiography was performed with special emphasis on number of vessels involved, percentage diameter stenosis, presence/absence of thrombus and TIMI flow grade (STEMI: infarct related artery was taken and unstable angina/NSTEMI: flow of culprit artery was noted). Congestive heart failure, hypotension (systolic blood pressure <90 mmHg), shock (cardiogenic shock and shock due to other cardiovascular causes including right ventricular myocardial infarction) and death were also determined.

Qualitative data were analysed using Chi-square test and quantitative data were analysed using independent t-test. All the data were analysed using SPSS version 20 (Chicago, IL, USA).

RESULTS

This study included total 103 patients and mean age of all the patients was 56.14 ± 11.04 years. Among all, 71 (68.9%) patients were >50 years old and 39 (31.1%) patients were ≤50 years old and of which majority of patients (37.86%) falls in the range of 51-60 years. Total 82 (79.6%) patients were presented with ST-segment elevation myocardial infarction (STEMI) which included 50 (61.73%) anterior wall STEMI and 32 (39.02%) presented as inferior wall STEMI and; other 21 (20.4%) patients were presented with unstable angina or non-ST segment elevation myocardial infarction. Among patients of inferior wall STEMI, 3 (9.37%) patients had right ventricular myocardial infarction. Baseline demography and laboratory findings of all the patients are outlined in Table 1.

The patients with ejection fraction ≤40% had higher WBC count (13,968 cells/mm^3) than those who had ejection fraction >40% (9,978 cells/mm^3) which is statistically significant ($p<0.0001$). Higher KILLIP class was associated with higher WBC count ($p=0.8379$). Higher WBC count was associated with increased incidence of congestive heart failure ($p<0.0001$) and associated with more number of diseased vessel ($p=0.0003$). Patients presented with shock ($p=0.0002$) and visualized thrombus during coronary angiography ($p<0.0001$) had a higher WBC count. Total WBC count in various conditions and the quantitative discrimination of WBC count in various conditions are outlined in detail in Table 2 and Table 3, respectively.

Parameters	n= 103 (Mean ± SD)
Age, years	56.14 ± 11.04
Total leucocyte count, cells/mm^3	10830 ± 3693.6
Pulse rate, beats/min	79.30 ± 13.61
Blood pressure, mmHg	119 ± 26.96
Creatinine, mg/dL	1.00 ± 0.29
Random blood sugar, mg/dL	117.46 ± 52.86
Total cholesterol, mg/dL	202.28 ± 42.370
High density lipoprotein mg/dL	45.29 ± 6.63
Triglyceride, mg/dL	151.01 ± 51.78
Low density lipoprotein mg/dL	133.10 ± 49.59
Creatine phosphokinase - myocardial band, IU/L	188 ± 113.81
Ejection fraction,%	49.99 ± 8.40

Table 1. Baseline Demography and Laboratory Findings of All the Patients

Parameters		No. of Patients (n=103)	Mean WBC Count (cells/mm^3)	P
Gender	Female	22	10505 ± 4689.9	0.6434
	Male	81	10919 ± 3403.5	
Diabetes mellitus	Yes	30	11573 ± 4036.9	0.1919
	No	73	10525 ± 3526.8	
Smoker	Yes	68	11188 ± 3856.2	0.1713
	No	35	10134 ± 3296.8	
Ejection fraction	≤40%	22	13968 ± 3012.3	<0.0001
	>40%	81	9977.8 ± 3401.3	
Congestive heart failure	Yes	30	13590 ± 3785.6	<0.0001
	No	73	9695.9 ± 3012.8	
Killip class	Class-II	10	13220 ± 2480.5	0.8379
	Class-III	9	13322 ± 3979.3	
	Class-IV	11	14145 ± 4776.3	
Shock	Yes	19	13632 ± 3890.5	0.0002
	No	84	10196 ± 3890.5	
Death	Yes	4	16450 ± 2301.4	0.0016
	No	99	10603 ± 3463.1	
LAD lesions	Yes	76	11392 ± 3864.6	0.0089
	No	27	9248.1 ± 2630.1	
Culprit vessel	Patent	77	10087 ± 3409.4	0.0003
	Non-patent	26	13031 ± 3686.1	
Thrombus	Yes	42	12650 ± 3423.5	0.0001
	No	61	9577 ± 3356.9	

Table 2. Mean WBC Counts in Different Conditions

WBC: White blood cells and LAD: left anterior descending artery

Parameter		Total WBC Category Group-1 (<10000 cells/mm^3)	Group-2 (10000-15000 cells/mm^3)	Group-3 (>15000 cells/mm^3)	P
CHF (n= 30)		5 (11.6%)	14 (31.1%)	11 (73.3%)	<0.0001
Shock (n= 19)		2 (4.6%)	8 (17.7%)	9 (60.0%)	<0.0001
Mortality (n= 4)		00	1 (2.2%)	3 (20.0%)	0.0029
Number of disease vessel	SVD (n= 52)	30 (57.7%)	20 (38.5%)	2 (3.8%)	0.0005
	DVD (n= 28)	11 (39.3%)	11 (39.3%)	6 (21.4%)	
	TVD (n= 23)	2 (8.8%)	14 (60.7%)	7 (30.5%)	
TIMI flow	Grade 0/1 (n= 21)	6 (13.5%)	12 (26.7%)	8 (53.4%)	<0.0001
	Grade 2 (n= 14)	2 (4.6%)	14 (31.1%)	4 (26.7%)	
	Grade 3 (n= 57)	35 (81.4%)	19 (42.2%)	3 (20.0%)	

Table 3. Categorical Differences in WBC Count in Different Conditions

WBC: white blood cells; CHF: congestive heart failure; SVD: single vessel disease; DVD; double vessel disease; TVD: triple vessel disease; TIMI: thrombolysis in myocardial infarction

DISCUSSION

The results of the present study confirm previous observations that relate elevated WBC count to adverse clinical outcomes and severe coronary artery lesions in patients with ACS and further explore the pathophysiology that underlies this relationship. In our study, baseline WBC count ranged from 4,200-20,000 cells/mm^3 (4.2 to 20×10^9 cells/L). So, our observation conforms to the findings of the previous studies.[7,8]

No correlation was found between total WBC count and age of patient (p=0.2097). Furthermore, total WBC count showed inverse correlation with ejection fraction with statistical significance, i.e. with increase in WBC count, there was a decrease in ejection fraction. In previous studies, the rise in creatinine kinase level after thrombolytic therapy was found to be more strongly associated with WBC count (1, 8, 9). We also found that total WBC count was positively correlated with creatine kinase myocardial band level, i,e. with increase in WBC count there was increase in serum creatine kinase myocardial band level which is statistically significant (p<0.0001). Our study showed an inverse correlation with ejection fraction and those patients with ejection fraction ≤40% had higher WBC count (13,968 cells/mm^3) than those who had ejection fraction >40% (9,978 cells/mm^3) which is statistically significant (p<0.0001).

Sabatine M S et al[7] in TACTICS-TIMI 18 sub-study found that the baseline WBC count was higher in patients who died within 30 days (p=0.0016) and within six months (p=0.0047). In our study, the development of new congestive heart failure or shock was associated with a higher WBC count. Moreover, when analysed according to WBC categories (<10,000 cells/mm^3, 10,000-15,000 cells/mm^3 and >15,000 cells/mm^3), we found that higher WBC category was associated with increased incidence of congestive heart failure, shock and in-hospital mortality (p value were <0.0001, <0.0001, 0.0029; respectively). We also found that higher WBC count was associated with lower TIMI flow grade (p<0.0001). Our study also found that those with totally occluded artery (TIMI 0/1) had higher WBC count than those with patent artery (TIMI 2/3) which is statistically significant (p=0.0003).

In TIMI-10 sub-study, Hal V. Barron et al.[8] did not find any association between the WBC count and percent diameter stenosis or minimum lumen diameter. Unfortunately, in this study we didn't compare percentage diameter stenosis of culprit artery with WBC count, but we found that more the number of diseased vessel, higher the WBC count (p=0.0005). Our study found that patients with left anterior descending artery lesion had higher mean WBC count (11,393 cells/mm^3) than those who did not had a left anterior descending artery lesion (9,248 cells/mm^3) with statistical significance (p=0.0089). We also found that patients with visualised thrombus during coronary angiography had higher mean WBC count than those without thrombus (12,650 cells/mm^3 vs 9,577 cells/mm^3; p=0.0001) which was in line with previous studies.[9,10]

Limitations

The main limitation of this study is small sample size. We did not collect information regarding the differential WBC count and its relationship with clinical outcomes and angiographic findings, which could have contributed more information. As the study was conducted at a tertiary care centre, most of

the patients were with complications which may have biased the results. Due to lack of availability of female beds, most of the patients were male, so there was a gender bias.

CONCLUSIONS

With growing body of evidence, now it is established that inflammation plays a pivotal role in atherosclerosis. We found that WBC count is a strong independent predictor of short-term mortality and morbidity in patients with ACS which further strengthens the links between inflammation and cardiovascular disease. In low resource setting, WBC count may become an additional parameter for the preliminary approach of ACS patients. However, in future more large studies are needed including both total WBC count and differential WBC count in different spectrum of ACS patients.

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