THE ONE MONTH OUTCOME OF PATIENTS WITH ACUTE CORONARY SYNDROME IN RELATION TO WBC COUNT
Dr. MOHAMAD SAEED ABDULZAHRA
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ABSTRACT

BACKGROUND:
Inflammation has been shown to play a role in atherosclerosis and CHD. An elevated leukocyte count is associated with adverse hospital outcome in patients presented with acute coronary syndrome.

OBJECTIVE:
This study was designed to determine the association between baseline total WBC count and the hospital mortality and complication (heart failure) in patients with ACS.
including STEMI, NSTEMI, and UA and to verify if this parameter has significant predictive power of clinical severity and outcome.

PATIENTS AND METHODS:
The relationship between baseline total WBC count, with hospital mortality and complication (heart failure) and clinical outcome in 57 patients with ACS admitted to the CCU in AL-SADAR teaching hospital from the first of April to the 30th of August 2007 has been tested. Diseases were evaluated for seventeen (17) patients with STEMI, twenty (20) patients with NSTEMI, twenty (20) patients with UA, venous blood samples were taken from each patient for baseline total WBC count, fasting lipid profile, random blood sugar. Comparison between those patients with STEMI, NSTEMI, UA were conducted includes one inflammatory marker (WBC).

RESULTS:
High total baseline WBC count was associated with high cardiovascular risk, heart failure and mortality (19.2%, 12.2%, and 8.77%) among patients with STEMI, NSTEMI, and UA respectively.

CONCLUSION:
In patients with ACS, initial leukocyte count is predictive of outcome and as the level increased the complications increase and the clinical outcome adversely affected.

INTRODUCTION
Leukocytes are the major cellular counterparts of inflammation and immunoreponse; they include neutrophiles, lymphocytes as well as monocytes, basophiles and eosinophiles. Inflammatory reaction may be blamed in the pathogenesis of coronary atherosclerosis. The role of WBC in atherosclerosis can be assessed simply by testing WBC count in the peripheral blood (1,2) the risk of acute MI is about four times as great in patients with WBC count high in the normal range > 9x10^9 cell/mm^3 as with patients with WBC count low in the normal range <6 x10^9 cell/mm^3, only 50% of this excess risk of high count individuals is explainable by tobacco (3,4). On the other hand, the benign constitutional neutropenia seen in certain ethnic groups appear to offer protection against atherosclerotic disease (5)

Over the last several decades an increase number of prospective studies conducted in CHD-free populations have clear’ and positive correlation between WBC count and risk of CHD, the correlation appear to persist even after adjustment of other risk factors (6). WBC count might play pathogenic role in vascular injury and might provide rough measure of the intensity of that process, the mechanism of this may be due to: 1- pressure-dependant plugging of micro-vessels, by intrinsically normal leukocytes. 2- rheological abnormalities of WBC including their formation of aggregate when activated 3- Endothelial cell injury (swelling and frank cytotoxicity or loss of substrate attachment) worked by WBC and their release products, toxic radicals, proteolytic enzymes and along acting oxidants. 4- pro-inflammatory cytokines result in expression of messenger cytokines like interleukin-4 which can travel from local site of inflammation to the liver where it trigger change in program of protein synthesis (8,9,10)

Leukocytes may influences the development of CHD via their ability to affect blood flow because their diameter are greater than the internal diameter of most nutritive capillaries, the rheological properties of WBC are major determinants of micro vascular perfusion, WBC exert an influence on blood flow disproportionate to their numbers because they are larger and stiffer than either RBC or platelets. WBC may obstruct small nutrient vessels (11,12, and I3)
follows necrotic injury usually render leukocytes less deformable and less able to pass through microvasculature thus aggravating ischemia, extending the infarct area and leading to further complications (14).

Leukocytes may influence the development of CHD by causing infarct expansion (14). During reperfusion of ischemic myocardium neutrophil and platelet can plug capillaries in the coronary microcirculation resulting in the no-reflow phenomenon, ventricular arrhythmias loss of vascular reserve, infarct expansion and even organ dysfunction (14,16,17). Leukocytosis might affect the state of hypercoagulability in response to acute MI and subsequent reperfusion. Also it might correlates positively with coagulation factors, including fibrinogen and factors VII and VIII (18, 19). Also it might involve the expression of certain cytokines (interleukin [IL-1, beta, IL-8, and IL-6) and adhesion molecules (macrophage adhesion molecule [MAC]-1) on circulating monocytes, which in turn leads to increased monocyte procoagulant activity (20,21). The leukocyte count appears to be a predictor of heart failure. In the TIMI-10A and –10B thrombolysis trials (23, 24) high leukocyte counts were significantly associated with the development of new CHF or shock, even after adjustment for potential confounding variables in a multivariate model.

**Patients and methods:**

The sample under study consists of eighty (80) patients presented with signs and symptoms of ACS admitted to the CCU of Al-Sadder teaching hospital from 1st of April to the 30th August, 2007. Only (57) patients of them completed the data of this study that were included. The remaining of them (23) patients didn’t came back for the second visit after one month for reevaluation so they are excluded from the study. Those 57 patients where classified into three groups according to their clinical criteria and ECG finding:

1. STEMI group (17)
2. NSTEMI group (20)
3. UA group (20)

The criteria for enrollment in this study include patients presented to CCU with chest pain ischemic in nature associated positive ECG finding in the form of ST-T changes and ST segment elevation. Because of the unavailability of cardiac enzymes (CBK, TROPONIN) so the classification of ACS were dependant on both history and ECG finding. Full history was taken stressing on risk factor include diabetes, hypertension, dyslipidemia, smoking. Diabetes was determined by fasting blood sugar level > 126 mg/dl or the use of antidiabetes drugs, hypertension was determined by physician-report for systolic blood pressure > 140 mmHg, diastolic blood pressure > 90 mmHg or use of anti-hypertensive agents. Dyslipidemia was determined by total cholesterol more than 200 mg/dl, smoking included active or previous >10 pack-years tobacco use, Clinical presentation included progressive chest pain started initially at rest lasting more than 20 minutes, chest pain with minimal exercise and presence or absence of pain in last 48 hours. According to the clinical presentation, patients classified in three group, STMI, NSTEMI, UA. After that patients underwent complete physical examination, following this venous blood sample was aspirated at the time of inserting I.V. line (before any medical intervention), first sample was anticoagulated with potassium 2 mg/dl EDTA, for WBC counting, second blood sample was taken for fasting blood sugar and cholesterol level. An expert lab personnel did WBC counting and patients were classified into three groups, thpse with low WBC count <6x10^9 cell/mm^3, intermediate WBC count 6x10^9cell/mm to 10x10^9cell/mm ,high WBC count >10x10^9/mm In the CCU daily follow up was arranged for all patients, stressing on the presence of complications that include recurrent ischemic chest pain.
Arrhythmia (VF, VT, AF, PVCs) and any symptoms and signs of LVD that involved (PND, orthopnoea, bilateral basal crepitation, increased JVP), echo study was arranged for all patients, LVEF, regional wall motion abnormality were assessed and echo study of LVD was documented, the patients were followed up daily in hospital and reevaluated 30 days after discharge from the hospital in the out patient department or by telephone call. Data were collected and analyzed by using SPSS (statistical package for the social sciences) version 10, Chi-square test used to compare between frequency variables, statistical significance considered when P-value < 005.

Results:
The study population consisted of 57 patients studied admitted to the OCU. The mean age of the patients was 55.8 years. Regarding sex distribution, male show higher figure than female, figures in male 37(65%), 11(19.2%) for STEMI, 11(19.2%) for NSTEMI, 15(26.3%) for UA, figures in female 20(35%), 6(10.5%) for STEMI 9(15.7%) for NSTEMI, (8.7%) for UA, as shown in (figure -1). There is no statistically significant difference between types of ACS with the presence or absence of hypertension, STEMI 8(14%), NSTEMI 10(17.5%), unstable angina 11(19.2%) as shown in (figure -2).

Smoking, seem to be more prevalent among patients with STEMI 14(24.5%), while more patients with unstable angina 8(14%) and NSTEMI 7(12.28%) were found to be non-smoker, but this does not show significant statistical difference as shown in (figure -3).

Many cases of unstable angina were shown to be non diabetic so far the STEMI, but the difference is less clear for NSTEMI, generally the difference is statistically non significant, UA 16 (28%), STEMI12(21%), NSTEMI11(19.2%), as shown in (figure-4).

The incidence of CHD associated with hyperlipidemic dose not show significant statistical result although its more in STEMI 6(10.5%) than NSTEMI 2(3.5%), and UA 3(5.2%) as shown in (figure -5). All patients with high count have complications, the complications are more among STEMI 11(19.2%) than NSTEMI 7(12.2%), and UA 5(8.77%), and the difference is statistically was significant as shown in (figure -6).

Patients with low count have no complications, patients with intermediate count show some complications 5(9%) while the remaining 24(42%) show no complication, according to this result higher baseline WBC count was a predictive of more sever clinical out come as shown in (Table- 1). There is three death only among patients with high count 25.%, and no death in those with low count (0.00%) and intermediate (0.00%) count this mortality difference is statistically significant as shown in (Table -2).
Figure-1 show the sex distribution

Df = 2

P value = 0.4
Figure- 2 show the relation of hypertension with the type of CHD

Chi-square =0.4

Df=2

P value =0.79
Figure-3 show the relation of smoking with types of CHD

Chi-square = 1.3
Df=2
P value = 0.5
Figure- 4 show the relation of diabetes mellitus with the types of CHD

\[ \text{Chi-square} = 2.9 \]

\[ \text{Df} = 2 \]

\[ P \text{ value} = 0.22 \]
Figure- 5 show the distribution of hyperlipidemia with types of CHD

Chi-square =4.14

Df=2

P value = 0.126
Figure- 6 show the distribution of complication in types of CHD

Chi-square = 5.94

Df = 2

P value = 0.05
Table -1 show the relation between the type of IHD and WC, WOC

<table>
<thead>
<tr>
<th>Type of IHD</th>
<th>No. of patients</th>
<th>LOW</th>
<th>INTER</th>
<th>HIGH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>WC%</td>
<td>WOC%</td>
<td>WC%</td>
</tr>
<tr>
<td>STEMI</td>
<td>17</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>20</td>
<td>0</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>UA</td>
<td>20</td>
<td>0</td>
<td>6</td>
<td>10.5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>57</td>
<td>100</td>
<td>10</td>
<td>17.5</td>
</tr>
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</table>

Table-2 relation between out come and total WBC count

<table>
<thead>
<tr>
<th>Total WBC count</th>
<th>Out come</th>
<th>Death</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Low</td>
<td>15</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td>Intermediate</td>
<td>30</td>
<td>53</td>
<td>0</td>
</tr>
<tr>
<td>High</td>
<td>9</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>95</td>
<td>3</td>
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Discussion

In the presenting study baseline WBC count was measured among 57 patients with ACS and the clinical outcome for those patients were observed for one month duration, we find a strong relationship among base line finding of simple relatively inexpensive and almost universally obtained test (WBC count) and clinical outcome. Our patients were only 57 while other studies (.Cinnie E Byrne et at, Mark I Furman. et al ) (25,26) take 732-8269 patients respectively.

Although there are many risk factors that affect the development of ACS like Hypertension, DM, smoking and hypertipidemia, the presenting study didn’t show statistically significant difference between these risk factors in relationship with base line WBC count and this might be due to limitation of the number of the sampling that had been tested in this study. Other studies didn’t mention any thing about risk factors of their impact on the level of WBC count in patients with ACS. (25,26).

Other studies (25, 26,27) classify their patients into four groups but we use three groups because of small number of cases and inability to perform statistical arrangement over small number in our study STEMI cases were 30% while in Mark I. Furman. et at study (26) NSTEMI 35% while in Mark I. Furman. et at study (26) 32%, UA 35% while in the study 31%.In our study most patients with high baseline WBC bount develop complications which include heart failure ,in STEMI 19.2% develop complications% while in Mark I.Furman. et at (26) 30.1% .in NSTEMI 12.2% while Mark I.Furman. et at (26) 34%, UA 8.7% white Mark I.Furman. et at (26) 22%. Although there are agreement in both studies for development of complications among patients with high baseline WBC count, but the discrepancy of the results between both studies could be explain by difference in the size of the sample.

In the presenting study three deaths had occurred and these are associated with high WBC count and there is no death with low and intermediate count. There are two deaths in STEMI 11.6% white in Mark I.Furman. et at study (26) 11.5%, and one in NSTEMI 5% while in Mark I.Furman. et at study (26) 8.5% and there is no death in UA while in Mark I.Furman. et at study (26) 7.1% this difference in death rate among patients with UA may be due to limitation of our study number. And this result is in agreement with other studies like Mark.Furman et at 26) in reporting that elevation of WBC count is associated with high incidence of death.

Study limitations:

This study was prospective in patient enrollment and follow-up but was observational in nature and subject to limitations, the restricted number of patients in our study affects the statistical result, and we hoped that cardiac enzymes are available in the future to increase the accuracy of diagnosis of ACS

Conclusions:

A high leukocyte count is associated with increased ACS-related morbidity and mortality. As the level of WBC count increased the risk of complication and mortality.

Recommendation:

Assessing the level of WBC count is an important variable in predicting an adverse out come in patients with ACS
References:
2. Libby P. Vascular biology of atherosclerosis overview and state of the art. Am J Cardiol 2003; 91:3A-6A.
21. Barron H, Cannon C, Murphy S, Braunwald E, Gibson C. Association between white blood cell count, epicardial blood flow, myocardial perfusion, and clinical outcomes in