

Elevated leukocyte count and adverse events in patients with acute coronary syndrome.

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الخلاصة

اجريت هذه الدراسة لمعرفة العلاقة بين معدل عدد كريات الدم البيضاء الكلي وحدوث المضاعفات ومعدل الوفيات عند المرضى المصابين بمتلازمة الشرايين التاجية الحادة ولمعرفة مدى تأثير هذه العلاقة على شدة الحالة السريرية. في هذه الدراسة تم اجراء فحص عدد كريات الدم البيضاء الى 57 من المرضى المصابين بمتلازمة الشرايين التاجية الحادة من المرضى الراقدين في وحدة انعاش القلب في مستشفى الديوانية التعليمي للفترة من شهر كانون الثاني 2008 لغاية 30 آذار 2008 وتمت متابعة المرضى خلال هذه الفترة وكان تقسيم المرضى المصابين الى ثلاث مجاميع حسب نوعية الاصابة وتمت مقارنة قراءات عدد كريات الدم البيضاء الكلي للمرضى اعلاه مع حدوث المضاعفات المرضية وكانت هناك ارتباط وثيق بين ارتفاع العدد الكلي لكريات الدم البيضاء عند المرضى المصابين بمتلازمة الشرايين التاجية الحادة وحدوث مضاعفات المرض السريرية.

Abstract

Inflammation has been shown to play a role in atherosclerosis and CAD. An elevated leukocyte count is associated with adverse in-hospital outcome and mortality in patients presented with acute coronary syndrome. This study was designed to determine the relation between initial total WBC count and the hospital mortality and complications in patients with ACS including STEMI, NSTEMI, and UA and to know if this parameter has significant power of clinical severity and outcome. Patients and methods: The relationship between initial total WBC count with hospital mortality and complications and clinical outcome in 57 patients with ACS admitted to the CCU in AD-DIWANYIA teaching hospital from the first of January to the 30 of March 2008 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 initial total WBC count, fasting lipid profile, random blood sugar. Comparison between those patients with STEMI, NSTEMI, UA were conducted includes one inflammatory marker (WBC). High initial total 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 immunresponse; they include neutrophiles, lymphocytes as well as monocytes, basophiles and eosinophiles. Inflammatory reaction may play a role 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 in the range $> 9 \times 10^9$ cell /mm³ as with patients with WBC count range $< 6 \times 10^9$ cell /mm³, only 50% of this excess risk of high count individuals is explainable by tobacco ^(3,4). Over the last several decades an increase number of prospective studies conducted in CAD-free populations have clear and positive correlation between WBC count and risk of CAD, the correlation appear to persist even after adjustment of other risk factors ^(6,7). WBC count might play pathogenic role in vascular injury and might provide rough measure of the intensity of that process. Leukocytes may influence the development of CAD 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, 13). In patients with acute MI the leukocytosis that 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 CAD by causing infarct expansion ⁽¹⁴⁾, during reperfusion of ischemic myocardium neutrophil 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 correlate 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 ^(20,21,22). 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, even after adjustment for potential confounding variables in a multivariate model.

Patients and methods

The sample under study consists of 57 patients presented with signs and symptoms of ACS admitted to the CCU of AD-DIWANYIA teaching hospital from 1st of January to the 30th March, 2008... Those patients were 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 that involve 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 and positive results of cardiac enzymes (CPK, TROPONIN). 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 random blood sugar > 200 mg/dl or the use of antidiabetes drugs; hypertension was determined by 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, According to the clinical presentation , patients classified in three group ,STMI, NSTMI, 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, those with WBC count $< 6 \times 10^9$ cell /mm³ , intermediate WBC count 6×10^9 cell /mm³ - 10×10^9 cell /mm³ , WBC count $> 10 \times 10^9$ /mm³ . In the CCU daily follow up was arranged for all patients ,stressing on the presence of complications that include recurrent ischemic chest pain , arrhythmia 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 echostudy of LVD was documented . 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 < 0.05.

Results

The study population consisted of 57 patients studied admitted to the CCU .The mean age of the patients was 55.8 ± 5.22 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(2.28%) 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 CAD 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)

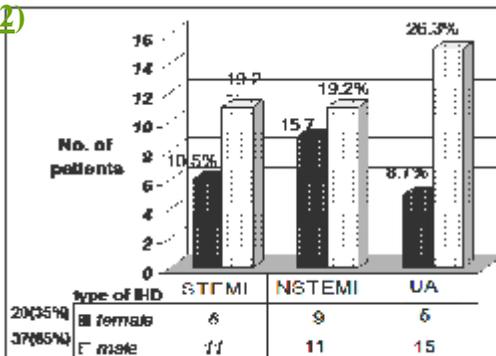


Figure-1 shows the sex distribution. (DF =2, P value =0.4)

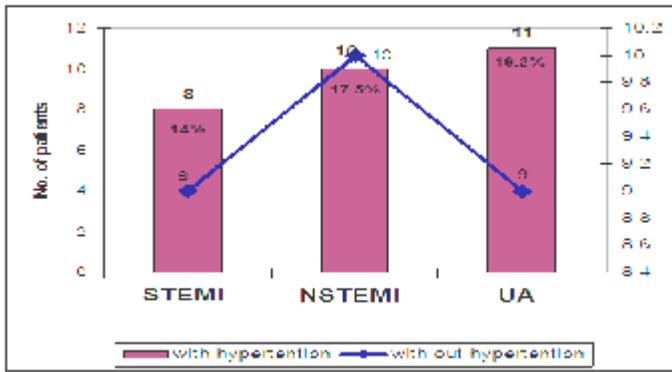


Figure- 2 shows the relation of hypertension with the type of CAD. (Chi-square =0.4 ,Df=2 ,P value =0.79)

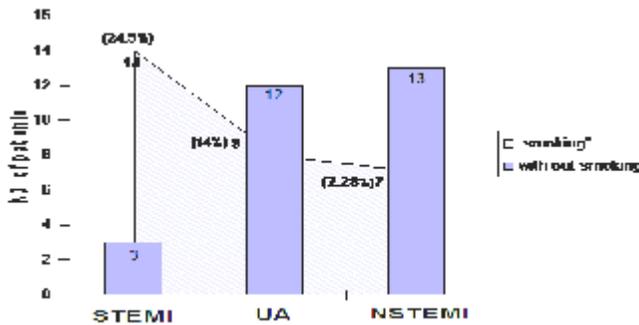


Figure-3 shows the relation of smoking with types of CAD. (Chi-square =1.3,Df=2,P value =0.5)

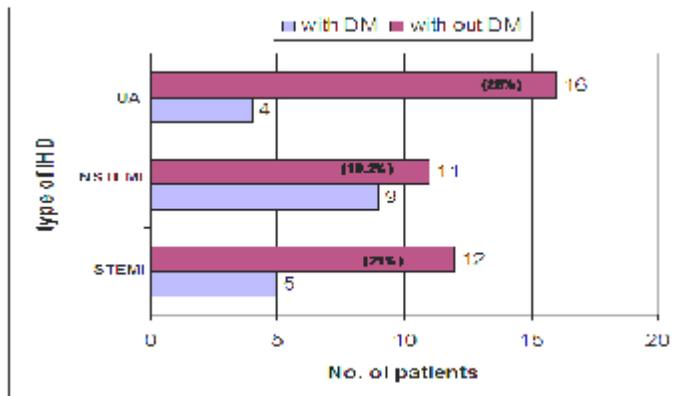


Figure- 4 shows the relation of diabetes mellitus with the types of CAD. (Chi-square =2.9,Df=2,P value =0.22)

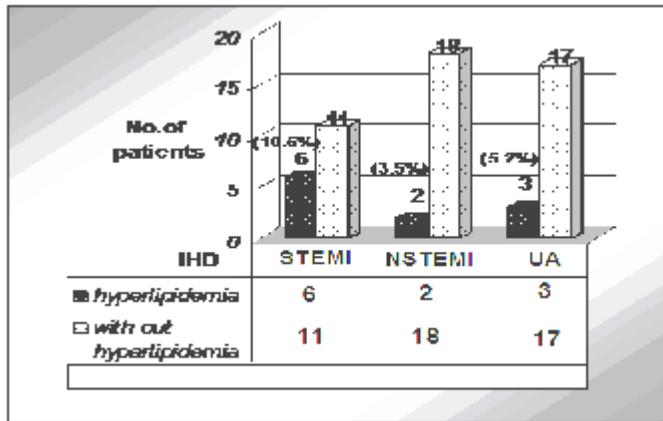


Figure- 5 shows the distribution of hyperlipidemia with types of CAD. (Chi-square =4.14, DF=2, P value = 0.126)

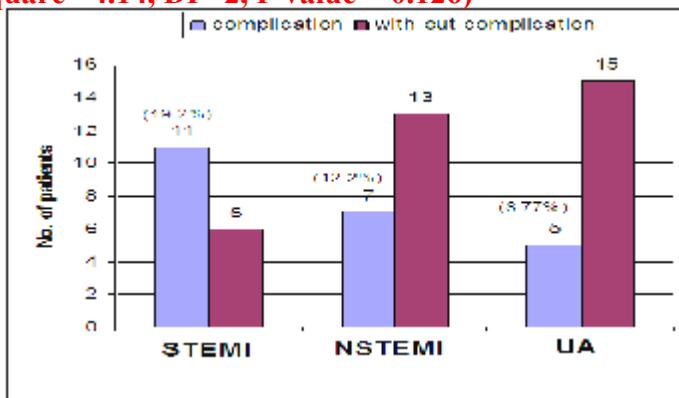


Figure- 6 show the distribution of complication in types of CAD (Chi-square =5.94, DF=2, P value =0.05)

Table -1 show the relation between the type of IHD and WC, WOC.

TYPE OF IHD	Nil of patients	%	LOW				INTER				HIGH			
			WC	%	WOC	%	WC	%	WOC	%	WC	%	WOC	%
STEMI	17	30	0	0	0	0	1	5	10.5	0	17.5	0	0	
NSTEMI	20	35	0	0	4	20	4	20	14	4	20	0	0	
UA	20	35	0	0	6	30	0	0	10	17.5	4	20	0	0
TOTAL	57	100	0	0	10	17.5	5	8	24	42	18	31.5	0	0

Table-2 relation between out come and total WBC count.

Total WBC count	Out come						p-value
	survive		Death		total		
	No.	%	No.	%	No.	%	
Low	15	26	0	0	15	26	0.0001
Intermediate	30	53	0	0	30	53	0.0001
High	9	16	3	5	12	21	0.08
Total	54	95	3	5	57	100	

Discussion

In the presenting study initial WBC count was measured among 57 patients with ACS, we find a strong relationship among base line WBC count and clinical outcome. Number of patients in this study are 57 while other studies (.Cinnie E Byrne et al, Mark I.Furman. et al)^(25, 26) take 732-8269 patients respectively .The presenting study didn't show statistical significant difference between risk factors in relationship with initial WBC count and this could be due to limitation in numbers of the sampling that had been tested in this study while in other studies there are relation between risk factors and 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 al study⁽²⁶⁾ 35% ,NSTEMI 35% while in Mark I.Furman. et al study⁽²⁶⁾ 32%, UA 35% while in the study 31%.In our study most patients with high initial WBC count develop complications, in STEMI 19.2% develop complications while in Mark I.Furman. et al⁽²⁶⁾ 30.1% .in NSTEMI 12.2% while Mark I.Furman. et al⁽²⁶⁾ 34%, UA 8.7% while Mark I.Furman. et al⁽²⁶⁾ 22%. Although there are agreement in both studies for development of complications among patients with high initial 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 (one due to VF and the other due to acute heart failure) 11.6% while in Mark I.Furman. et al study⁽²⁶⁾ 11.5%, and one in NSTEMI(due to acute heart failure) 5% while in Mark I.Furman. et al study⁽²⁶⁾ 8.5% and there is no death in UA while in Mark I.Furman. et al 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 al ⁽²⁶⁾ in reporting that elevation of WBC count is associated with high incidence of death.

Study limitations

The restricted number of patients in this study might affect on the accuracy of results.

Conclusions

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

Recommendation

Assessing the level of WBC count is an important variable in predicting an adverse out come in patients with ACS .

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