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Relationship between White Blood Cell Count and Mortality in Patients with Acute Ischemic Stroke

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Abstract

***Background*:** Stroke is the most frequent and highly fatal neurologic disease. Many clinical symptoms and paraclinical methods have been suggested have a prognostic value in stroke, including the shift in white blood cell (WBC) count which has attracted much attention at the moment. The objective of this study is to assess the prognostic value of admission-time WBC count of patients with acute ischemic stroke on their hospital mortality in Rafsanjan.

***Materials and Methods*:** This is a descriptive-cross sectional study on 200 patients with acute ischemic stroke, that the diagnosis was confirmed with neuroimaging. WBC count during the first 12 hours of admission was assessed. Subsequently, the patients were divided in 2 groups of normal WBC count and high WBC count and followed until discharge or death. The data were analyzed statistically using Fisher Exact test.

***Results*:** In our study, 54% of our patients were men and the others were women. 17.5% of patients had abnormal WBC count. 27 patients (13.5%) were expired, consisting of 5 patients with increased WBC count and 22 with normal WBC count. No significant relationship was observed between the WBC count and hospital mortality. Also, no significant relationship was observed between the WBC count and hospital mortality in terms of age and gender.

***Conclusion*:** The findings of our study show that WBC count doesn't have any predictive value on hospital mortality in patients with ischemic stroke.

Introduction

Stroke is the most frequent and highly fatal neurologic disease. Most patients suffer from long-term its complications or recurrence [1]. Following stroke, patients and their family are confused about long-term prognosis of their disease. Today, a wide range of clinical symptoms and paraclinical methods have been suggested as prognostic predictors for patients with stroke, the values of each of them is unclear. These predictors include level of consciousness, severity of primary symptoms, history of stroke or cardiac attack, presence of background diseases such as diabetes and hypertension, age, gender, obesity, changes in electrocardiograph or electroencephalograph, severity of lesion on imaging, etc, but the sensitivity and specificity of these factors are low [2-7]. One indicator, which is attracting attention today, is the shift in WBC count of patients with stroke. For example, in one study in the United States on 192 cases, the WBC count on admission was higher than normal in dead patients, suggesting a prognostic value for WBC count [8]. Another study in Dutch on patients suffering from stroke indicated that high WBC count during the first 12 hours of admission was associated with higher mortality during short-term follow-up [9]. Also, in another study on 100 patients in acute phase of stroke authors reported that high WBC count of the first day is associated with higher mortality, but not morbidity [10]. In contrast, some studies failed to identify WBC count as a predictive factor for ischemic stroke [3, 4, 11, 12]. Verification of the role of WBC as an early prognostic factor of functional outcome after ischemic stroke may be of clinical importance, because it is an easily-measured and readily available inflammatory marker. Considering above controversy about its prognostic value, we decided to evaluate the prognostic value of admission-time WBC count of patients with acute ischemic stroke on their hospital mortality in Rafsanjan.

Materials and Methods

This is a descriptive- cross sectional study on 200 ischemic stroke patients referring to Ali-Ebn-e-Abitaleb Hospital, Rafsanjan, from June 2009 to March 2010. Sampling was done using the convenience method. The time of onset of the stroke was defined as the time when the patient or observer first became aware of the symptoms and blood samples for assessment of WBC count were obtained during the first 12 hours of disease,

before starting any intravenous infusion. Subsequently, all patients underwent cerebral CT-scan and MRI (except some cases such as patients with heart synthetic valve). If necessary, contrast materials were used for confirming the diagnosis of ischemic stroke. (Stroke was defined, as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than of vascular origin) [1]. If there was history of stroke, systemic diseases (including blood dyscrasies and vacuities) drug consumption (except medication for hypertension, diabetes, cardiac ischemia or arrhythmia) the patient were excluded from our study. Other exclusion criteria were fever on admission, abnormality of other laboratory tests, such as urea, creatinine, hepatic enzymes, and erythrocyte sedimentation rate, leucopenia (less than 3500/ml) or leukocytosis more than 25000/ml [13].

A specialist in infectious diseases supervised the entire procedure. Subsequently, the patients were treated according to the standard treatment protocols of our hospital.

The study in no way interfered with the treatment. Subsequently, based on their WBC count, the patients were divided in 2 groups, normal WBC or leukocytosis (leukocyte count ≥10000) [14]. Cerebrovascular risk factors such as cigarette smoking (any subject whose smoking index was more than 200); hypercholesterolemia (history of hypercholesterolemia and/or fasting total cholesterol level>200 mg/dL); hypertriglyceridemia (history of hypertriglyceridemia and/or fasting triglycerides level>180 mg/dL); arterial hypertension (history of hypertension and/or systolic blood pressure >150 mm Hg and/or diastolic pressure >90 mm Hg, out of the acute phase, treated or not); and diabetes mellitus (history of diabetes and/or FBS>126 mg/dl, out of the acute phase, treated or not) were screened [15].

They were followed to assess for hospital discharge or death. The study protocol was approved by the Institutional Ethics Committee in Rafsanjan medical university. In this study confidence interval (CI) were calculated at the 95% level and the data were recorded in SPSS software version 16, and analyzed using statistical method Fisher Exact test. For all statistical analyses, a value of $p<0.05$ was considered to indicate significant difference.

Results

In this study, 54% of our patients were men and the others were women. The mean age was 70.32±5.6 years for women and 64.25±5.7 years for men. The range of age was from 28 to 98 years. 34% of patient had lacunar infarction, 18% of patient had cardioembolic infarction and 48% of patient had large vessel atherosclerotic infarction. In this study, 17.5% of participants had abnormal white blood cells. 27 patients (13.5%) were expired, consisting of 5 patients with increased WBC count and 22 patients with normal WBC count. No significant relationship was observed between the WBC count and hospital mortality in patients with acute stroke. Furthermore, no significant relationship was observed between the WBC count and hospital mortality in terms of age and gender (Table 1 and 2). Hypertension and dyslipidemia were the most frequent cerebrovascular risk factors in this study (Table 3).

Table 1. Frequency of study units in terms of age groups and mortality

Age	Normal WBC count		Abnormal WBC count		Total N(%)	Fishers Exact Test
	Death N(%)	Discharge N(%)	Death N(%)	Discharge N(%)		
Under 40	2(13.3)	8(53.3)	0(0)	5(33.3)	15(100)	*p*= 0.5238 OR= 3.235 95% CI=0.1291-81.057
40-49	2(7.41)	19(70.4)	1(3.7)	5(18.52)	27(100)	*p*= 0.5453 OR= 0.5263 95% CI= 0.03927-7.054
50-59	5(10.42)	39(81.25)	1(2.1)	3(6.25)	48(100)	*p*= 0.4248 OR= 0.3846 95% CI 0.03326-4.447
60-69	4(7.01)	43(75.44)	2(3.5)	8)(14.04)	57(100)	*p*= 0.2814 OR= 0.3721 95% CI= 0.05804-2.386
Over 70	9(12)	56(74.67)	1(1.33)	9(12)	75(100)	*p*= 0.995 OR= 1.446 95% CI= 0.163-12.836

Table 2. Frequency of study units in terms of gender and mortality

Gender	Normal WBC count		Abnormal WBC count	
	Death N(%)	Discharge N(%)	Death N(%)	Discharge N(%)
Male	14(63.6)	74(51.7)	3(60)	17(56.7)
Female	8(36.4)	69(48.3)	2(40)	13(43.3)
Total	22(100)	143(100)	5(100)	30(100)
Fishers Exact Test	*p*=0.362 OR= 1.632 95% CI= 0.645-4.131		*p*=0.998 OR= 1.632 95% CI 0.645 to 4.131	

Table 3. Frequency of stroke risk factors in patients

Risk factor		Death N(%)	Discharge N(%)	Total N(%)	*p*-Value
Heart disease	yes	7(17.07)	34(82.93)	41(100)	0.448
	no	20(12.58)	139(87.42)	159(100)	
Hypertension	yes	16(16.84)	79(83.16)	95(100)	0.2172
	no	11(10.48)	94(89.52)	105(100)	
Diabetes	yes	12(20.69)	46(79.31)	58(100)	0.069
	no	15(10.56)	127(89.44)	142(100)	
Dyslipidemia	yes	15(17.86)	69(82.14)	84(100)	0.145
	no	12(10.34)	104(89.66)	116(100)	
Smoking	yes	6(17.65)	28(82.35)	34(100)	0.417
	no	21(12.65)	145(87.35)	166(100)	

Discussion

In this study the prognostic value of WBC count has been evaluated. 17.5% of our patients had abnormal WBC count, among which 5 expired in hospital. Statistical analysis indicated no significant relationship between WBC count and hospital mortality in patients with acute stroke. Some studies confirm our findings. For example, Zia in a prospective cohort study on 26,927 patients with acute stroke in 2012 showed that, there isn't any association between leukocyte count and mortality for either stroke subtype [11]. In another study in 2005 in Sweden, the researchers recruited 844 patients who had a stroke in Edinburgh.

The authors as same as us found that the WBC count does not have ability to predict outcome after stroke for this cohort of patients [16]. Also such as us, Koton in another study on 1,079 first-ever ischemic stroke patients in 2004 showed that cumulative mortality rates were 9.9% at 1 month and mortality of patients didn't have any correlation with WBC count [12]. Also, Szczudiik et al. in a cohort study (1 month) in Poland [3] and Heuschmann et al. in Germany showed that WBC count does not have important prognostic value [4].

Despite these studies and similar our findings, some studies have shown that leukocyte count independently predict mortality in patients with ischemic stroke for example, Peng et al. in an cohort study in China in 2010 showed that increased WBC count at admission was significantly and positively associated with in-hospital death or dependency at discharge among patients with acute cerebral infarction [14]. Also, Nardi et al. study in Italy showed that, elevated leukocyte count in the acute phase of cerebral ischemia is a significant independent predictor of poor initial stroke severity, poor clinical outcome after 72 hours, and discharge disability [17]. Other studies in the, Netherlands, Germany and the United States indicate that high count of WBC in patients with acute stroke is associated with higher mortality rates in short term [7-9, 13].

In a 5-year study in 3103 American participants of normal population, those with higher WBC count at the onset of study were more likely to expire due to involvement of cardiac or cerebral vasculature [18]. In another 8-year follow-up in an American population of 13,555 people, the risk of stroke was 1.9 times greater in people with higher WBC count [19]. Other American studies using doppler sonography of carotid arteries indicate that in patients with stroke or transient ischemic attack, higher WBC count are associated with increases size of the atheroma plaque in aorta [20, 21]. Some studies indicate this increased risk to be isolated, and others indicate it to be associated with other factors, such as hyperglycemia [22-25].

The cause of discrepancy between our results (and also Zia et al. [11], Koton, et al. [12] studies) with these opposite studies [9, 13, 14] is not clear. A main part of this difference may be related to frequency of kind of ischemic stroke in our population. The inflammatory and thrombotic components in ischemic stroke are of current interest, and there is some experimental evidence that they may be linked [7-26]. This correlation supports the hypothesis that there may be a link between these markers of inflammation, hypercoagulability, and fibrin turnover, respectively, in ischemic stroke patients, which may be associated with an unstable atherosclerotic condition that can increase the risk of future cerebrovascular and cardiovascular events. However, the correlation is not strong especially for lacunar infarction, which suggests that other factors have different effects on the levels of these variables [7-27].

These findings may be explained different results in studies especially our study, because in our study 38% of patient had lacunar infarction that is higher than other studies. Several mechanisms by which leukocytes may be implicated in parenchymal brain injury include vessel plugging, release of hydrolytic enzymes, oxygen free radicals or initiation of thrombosis [28-29]. Leukocytosis might also be a manifestation of some common causes of fever (e.g., pulmonary or urinary tract infections, sepsis, or pulmonary embolism from deep vein thrombosis) [13-28]. The short period of follow-up may partly account for the discrepancy between our findings and those of other studies. We also did not calculate hospital staying period and this is another limitation of study that maybe have influence on our findings.

In conclusion, although, our findings indicate that WBC counts do not have any predictive value on hospital mortality in patients with ischemic stroke but there are some strong studies with opposite findings. It seems that we need more studies to get a definite answer to this controversy.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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