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The effect of admission neutrophil/lymphocyte ratio on mortality in patients admitting to Emergency Department with spontaneous subarachnoid haemorrhage.

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Abstract

Objective: There are a lot of studies searching parameters and markers which are effective on prognosis and mortality in subarachnoid haemorrhage. But there aren't any studies about the effectiveness of Neutrophil Lenfosit Ratio (NLR) on mortality.

Materials and methods: In our study, former information of one hundred and thirty one patients who applying for varied complaints to our emergency service between January 2010 and April 2013 and diagnosed subarachnoid haemorrhage was analysed back and worked on study. The patients were categorized into two groups, namely the deceased and surviving groups.

Results: The most frequent designated complaint was headache (51.1%). Anterior comminican artery anevrism was the most seen (28.2%) and the most mortal (38.8%) developed anevrism in subarachnoid haemorrhage. The conditions of patients who were unconscious in the course of applying developed more mortal. NLR was found 7.71 ± 6.59 among survivor patients; 16.23 ± 12.68 among dead patients. Neutrophil lenfosit rate was found considerably high among dead patients compared to survivor patients.

Conclusion: In consequence, compared to other parameters Neutrophil lenfosit rate can be used as a simple, easy, and cheap parameter to guess short term prognosis and mortality. Doing more comprehensive and more studies will guide for the reason of high rates in NLR and the treatment of it.

Keywords: Subarachnoid haemorrhage, Neutrophil lenfosit ratio, Mortality.

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Introduction

Brain haemorrhage into subarachnoid space usually of arterial but rarely of venous origin is referred to as Subarachnoid Haemorrhage (SAH) [1,2]. From a clinical standpoint, SAH is categorized into traumatic and non-traumatic (spontaneous) varieties. In general, head trauma is the leading cause of SAH. On the other hand, the most common cause of non-traumatic SAH is intracranial aneurysm rupture. It is a type of haemorrhagic stroke and constitutes 6-8% of all strokes [3]. Its annual incidence ranges between 10 and 16 per 100.000 population, with the rates going higher with advancing age [1,2].

Mortality of SAH is affected by certain factors including age, admission symptoms, aneurysm localization, neurological status, and presence of comorbid disorders. Inflammatory process is known to play a significant role in all stages of atherosclerosis [4]. Previous studies indicating inflammation as a basic mechanism underlying vascular aneurysm formation have brought forward the question whether inflammation plays a role in mortality of SAH [5]. Currently, neutrophil/ Lymphocyte Ratio (NLR) is regarded as a parameter reflecting the combined unfavourable effects of both elevated neutrophil count indicative of acute inflammation, and reduced lymphocyte count indicative of physiological stress. NLR has been used by many recent studies as a simple, low-cost inflammatory marker. We studied NLR in whole blood to determine the effect of inflammation on mortality of SAH.

Materials and Methods

Our study was approved by Dicle University Faculty of Medicine Ethics Committee for a retrospective analysis of the medical information of patients presenting to Dicle University Faculty of Medicine Emergency Department with spontaneous subarachnoid haemorrhage between January 2010 and April 2013. It included patients older than 18 years who admitted to our emergency department with various symptoms and were diagnosed with SAH by Brain Computerized Tomography (BCT), Magnetic Resonance Imaging (MRI) and Lumbar Puncture (LP), and who also had complete blood count results. The exclusion criteria were presented on Table 1.

Patients' age, sex, pulse rate, arterial blood pressure, respiratory rate, consciousness state, comorbid disorders Diabetes Mellitus (DM), Hypertension (HT), habits (alcohol, smoking), complete blood count (leucocyte, haemoglobin, neutrophil, lymphocyte, thrombocyte counts), coagulation parameters (Prothrombin Time Test (PTT), Activated Partial Thromboplastin Time (APTT), internasyonal Normalized Ratio (INR), tools of diagnosis (BCT, LP), presence and localization of aneurysm(s), haemorrhage site, applied treatment (medical, surgical), and outcome (deceased, surviving) were analysed. The patients were categorized into two groups, namely the deceased and surviving groups. Parameters considered to be significant predictors of mortality were compared between the two groups.

Statistical analysis

Univariate analyses were done using Chi-square test (χ^2) for categorical variables and Student's t test for continuous variables. Average values were presented as Mean ± SD (standard deviation). A p-value of less than 0.05 was considered statistically significant.

Table 1. *Exclusion criteria.*

Exclusion criteria
Traumatic SAH
Undergoing surgical operation
Severe hepatic or renal disease
Acute metabolic disorder
Haematological disease
Missing medical information in hospital's automation system
Intracranial tumor
Active infection
Inflammatory disorders
Immunosuppressive use

Results

One hundred and thirty-one patients who admitted to our emergency department with spontaneous subarachnoid haemorrhage and who met the inclusion criteria were retrospectively evaluated. Eighty-two (62.5%) patients survived and 49 (37.5%) of them died. Seventy (53.4%) patients were female and 61 (46.6%) were male. The mean age was 52.88 ± 14.79 years (18-82 years). Of the deceased patients, 26 (53.1%) were female and 23 (46.9%) were male, and their mean age was 54.76 ± 15.50 years.

Sixty-seven (51.1%) patients presented with headache, 43 (32.8%) with loss of consciousness, 5 (3.8%) with seizure and syncope, and 16 (12.2%) with coma. Of the survivors, 54 (65.9%) had headache while 21 (42.9%) of the deceased ones had loss of consciousness. According to the findings of physical examination, 56 (42.2%) of the patients had stiff neck. Of the deceased ones, 10 (20.4%) had stiff neck. The distribution of the patients by presenting symptom and findings of physical examination were presented on Table 2. While presence of headache was a significant predictor of survival, coma and stiff neck were significant predictors of mortality (for each, $p<0.001$).

Fifty-one (38.9%) of our patients had hypertension. Twenty-seven (55.1%) of the deceased patients had hypertension. Table 2 shows the past history information of the study population. Having hypertension was significantly predictive of mortality ($p=0.005$).

Ninety-seven (74%) of our patients had aneurysm. Aneurysm was present in 39 (79.6%) of the deceased patients. 37 (28.2%) of the patient population had an anterior communicating artery aneurysm and 18 (13.7%) had a left MCA aneurysm. Of the deceased ones, 19 (38.8%) had an anterior communicating artery aneurysm. Sixteen (19.5%) of the surviving patients had a left MCA aneurysm. Distribution by aneurysm presence and localization shown by CT angiography examination was presented on Table 3. While aneurysm presence in anterior communicating artery was significantly predictive of mortality, left MCA aneurysms were predictive of a better survival ($p=0.046$ and $p=0.017$, respectively).

Table 4 presents study population's distribution by complete blood count and bleeding panel results. An elevated lymphocyte count was a significant predictor of survival ($p=0.001$). Elevated leucocyte, neutrophil counts and NLR were significant predictors of mortality (for each, $p<0.001$). We studied thrombocyte count, PTZ, aPTT, and INR levels in the bleeding panel but we did not observe any significant effect thereof on mortality.

Table 2. *Distribution of the study population by age, sex, clinical properties, and comorbid disorders.*

	Surviving (n=82)	**Deceased (n=49)**	**P-vaue**
Age	51.78 ± 14.31	54.76 ± 15.50	0.277
Sex			
Male	38 (46.3%)	44 (53.7%)	1
Female	23 (46.9%)	26 (53.1%)	

Presenting Complaint			
Headache	54 (65.9%)	13 (26.5%)	<0.001
Loss of consciousness	22 (26.8%)	21 (42.9%)	0.083
Seizure-Syncope	5 (6.1%)	--	0.156
Coma	1 (1.2%)	15 (30.6%)	<0.001
Examination findings			
Stiff Neck	46 (56.1%)	10 (20.4%)	<0.001
Babinski sign	8 (9.89%)	5 (10.2%)	1
Lateralizing sign	10 (12.2%)	5 (10.2%)	0.785
Comorbid disorders and habits			
Hypertension	24 (29.3%)	27 (55.1%)	0.005
Diabetes	10 (12.3%)	10 (20.4%)	0.223
Medication use	33 (40.2%)	29 (59.2%)	0.047
Smoking	33 (40.2%)	23 (46.9%)	0.471
Alcohol	4 (4.6%)	2 (4.1%)	1

Table 3. *Distribution by aneurysm presence and localization shown by CT angiography examination.*

CT angiography finding	**Surviving n=82**	**Deceased n=49**	**p**
Aneurysm			
Present	58 (70.7%)	39 (79.6%)	0.307
Absent	24 (29.3%)	10 (20.4%)	
Aneurysm localization			
Anterior communicating artery	18 (22.0%)	19 (38.8%)	0.046
Right MCA	17 (20.17%)	9 (18.4%)	0.823
Left MCA	16 (19.5%)	2 (4.1%)	0.017
Internal cerebral artery	7 (8.5%)	5 (10.2%)	0.762
Basilar artery	2 (2.4%)	2 (4.1%)	0.63
Vertebral artery	2 (2.4%)	1 (2.0%)	1
Posterior communicating artery	1 (1.2%)	--	1
Posterior cerebral artery	--	1 (2.0%)	0.374

Table 4. *Distribution of the study population by complete blood count and bleeding panel results.*

Parameter	**Surviving n=82**	**Deceased n=49**	**p**
Leucocyte count (K/uL; Mean ± SD)	11.97 ± 3.88	18.16 ± 5.80	<0.001
Haemoglobin (g/dL; Mean ± SD)	13.34 ± 2.00	13.92 ± 1.85	0.098
Neutrophil count (NULL; Mean ± SD)	9.53 ± 3.89	16.02 ± 5.11	<0.001
Lymphocyte count (NULL; Mean ± SD)	1.73 ± 0.93	1.27 ± 0.66	0.001
NLR(%; Mean ± SD)	7.71 ± 6.59	16.23 ± 12.68	<0.001
Thrombocyte count (K/uL; Mean ± SD)	264.43 ± 76.36	273.49 ± 85.35	0.543
PTT (INR; Mean ± SD)	12.31 ± 3.09	12.68 ± 1.46	0.359
aPTT (sec; Mean ± SD)	22.78 ± 5.54	24.53 ± 5.16	0.071
INR (Mean ± SD)	1.09 ± 0.46	1.12 ± 0.21	0.59

Discussion

SAH can affect persons of all ages although it is more common in advanced age. It has been reported that SAH is most prevalent between 40-60 years of age [6,7]. Two retrospective studies by Binatli et al. and Ilhan et al. consisting of 273 and 328 cases, respectively, indicated that SAH was more common between 40 and 60 years of age [8]. Our study showed a mean age of affected patients similar to those reported in the literature. Literature studies have reported conflicting information regarding the relationship between age and SAH's prognosis. Some series have reported that advanced age is an adverse prognostic factor [9]. In a study on 299 patients, the mortality rate of patients aged less than 60 years was 29% whereas it was 33% in those aged 60-70 years, and 55% in those aged above70 years [10]. Unlike that study, a 172-case study by Wang et al. revealed a mean age of 45.1 ± 12.2 years for survivors and 47.8 ± 11.2 years for those who died, indicating no significant effect of age on mortality [11]. Our study agreed with that of Wang et al [11].

Studies have demonstrated that SAH is more common in women [8,12]. Although our study did not indicate a significant difference between SAH prevalence in men and women, it was more prevalent in women, as suggested by the literature.

Different series to date have mentioned headache as the most common presenting symptom of SAH. Consciousness state has been specified as the leading factor predicting prognosis [13-15]. Headache was the presenting symptom in 70.2% of patients in the study of Ilhan et al. and 63.4% in that of Binatli et al. [8,12]. In a study comprising 104 cases, Eroglu et al. reported that 61 patients presented with loss of consciousness, of whom 29 (47.3%) died; analysis of the study data showed that loss of consciousness had a significant effect on mortality [16]. Binatli et al., in a study involving 273 cases, found that 45.4% of the patients had stiff neck, of which 67 later died. The authors concluded that stiff neck was a significant predictor of mortality [12]. In agreement with the literature, our study showed that headache was the most common presenting symptom. Headache had a significant favourable effect on survival while mortality of patients with loss of consciousness and stiff neck were significantly higher as suggested by literature data.

Risk factors for SAH include hypertension, smoking, oral contraceptive use, diabetes mellitus, excessive alcohol intake, diurnal changes in blood pressure, family history for SAH or aneurysm, genetic disorders, pregnancy, advanced age, and cocaine use [17,18]. Two studies by Binatli et al. and Ilhan et al. consisting of 273 and 328 cases, respectively, found that HT

was significantly effective on mortality [8,12]. In accordance with literature data, our study also revealed that our patients most commonly had a history of hypertension and smoking. On the other hand, DM, smoking, and alcohol use had no significant effect on mortality, HT was significantly predictive of mortality, as reported in the literature.

The leading cause of subarachnoid bleeding is intracranial aneurysm, which affects 2% of the general population. Subarachnoid haemorrhage not caused by aneurysm rupture has a more favourable prognosis and a lower rate of recurrent haemorrhage. Localization and site of an aneurysm is of great importance for prognosis [19,20]. Ilhan et al. reported that 83.1% of their patients had aneurysm, of which 32% had an ACA aneurysm [8]. Our study was in agreement with the literature reports. Aneurysm located in left MCA was significantly more favourable for survival. In a study involving 251 subjects, Canbaz et al. investigated the effect of aneurysm localization on mortality. The patients with aneurysms located in ACA (22.8%) had the highest mortality rate [21]. We also found that ACA aneurysms were predictive of mortality.

White blood cell count, neutrophil, lymphocyte counts, and neutrophil/lymphocyte ratio are markers of systemic inflammation. NLR is a simple, low-cost inflammatory marker recently used by many studies. Blood in subarachnoid space triggers an inflammatory reaction and causes an increased neutrophil and macrophage migration to the site of inflammation in the first 48 hours [22]. The effect of NLR on mortality in subarachnoid haemorrhage has not been studied. A few studies have investigated the effects of NLR on mortality after stroke and coronary artery bypass surgery [23,24].

Gokhan et al. studied 868 subjects to investigate the effect of NLR on mortality in stroke and transient ischemic attack. They found that neutrophil, lymphocyte count, and NLR were significant predictors of mortality [23]. In another study, Unal et al. explored the role of NLR in prediction of mortality after coronary artery bypass surgery in 210 patients and found that NLR was a significant predictor of mortality [24]. Eren et al. found a positive correlation between NLR and admission GRACE score and a positive correlation of borderline significance between STEMI TIMI risk score and NLR, but failed to show a significant difference between NLR groups with respect to in-hospital mortality as well as mortality and hospital admissions form cardiac causes at 6 months and during the whole follow-up. Ayhan et al. found a significantly higher NLR in patients with coronary artery ectasia [25]. We also found that higher leucocyte and neutrophil counts and NLR ratio were significant predictors of mortality.

Conclusion

NLR can be used to predict short-term prognosis and mortality in spontaneous subarachnoid haemorrhage as a simpler and cheaper parameter than other parameters.

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Author's Contribution

Each of the authors contributed to the research, data analyses and writing. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no competing interests.

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