Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

ORIGINAL ARTICLE

PREDICTIVE VALUE OF NEUTROPHIL TO LYMPHOCYTE RATIO AND SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE IN PATIENT WITH SEPSIS

SAHED UDDIN AHMED[1], MD. ABU HANIF CHOWDHURY[2], MD. JABER ABEDIN[2], MA SATTAR[3], SUJAT PAUL[4], ASOK KUMAR DUTTA[4]

Abstract:

Background: *Neutrophil to lymphocyte ratio calculated from white cell differential count provides a rapid indication of the extent of an inflammatory process. The aim of the study was to evaluate the predictive value of neutrophil to lymphocyte ratio and SOFA score in sepsis outcome.* ***Methods:*** *Adult patients presenting to medicine department of CMCH with suspected sepsis by qSOFA score were considered for the present study. Baseline qSOFA, SOFA Score and NLR were calculated. Patients were followed until discharge or death to observe outcome. The primary outcome was in-hospital mortality. Secondary outcomes were ICU referral and ICU stay. All data were prospectively collected, coded and tabulated. ROC curves were constructed to evaluate the performance of NLR and SOFA in differentiating non-survivors from survivors. Multivariate logistic regression analysis was done to determine the independent predictors adjusted for the previously specified baseline covariates.* ***Results:*** *The AUC for each indicator was compared. NLR had a modest power for predicting unfavorable outcome (death) as suggested by AUC of 0.705 (95% CI: .556-.854), which was greater than that of baseline qSOFA score (0.694). NLR ≥8.9 was proposed as the optimal cutoff value, which provided a sensitivity of 75.0% and a specificity of 67.7% for predicting mortality in sepsis. After adjusting for other variables NLR and SOFA remain as independent predictors of unfavorable outcome. Baseline NLR also had a modest power for predicting need for ICU referral than that of baseline SOFA score.* ***Conclusion:*** *NLR is an easily calculated, simple, cost-effective index that could be used as a prognostic tool for clinicians when assessing sepsis patients in the emergency department and general ward.*

Key words: *NLR, SOFA score, Sepsis.*

Received: 15.02.2023 *Accepted: 10.04.2023*
DOI: https://doi.org/10.3329/bjm.v34i2.65686

Citation: *Ahmed SU, Chowdhury MAH, Abedin MJ, Sattar MA, Paul S, Dutta AK. Predictive Value of Neutrophil to Lymphocyte Ratio and Sequential Organ Failure Assessment Score in Patient with Sepsis. Bangladesh J Medicine 2023; 34: 86-92.*

Introduction:

Sepsis is one of the most common causes of multi-organ failure and still a big challenge to both the developed and developing world. The reported morbidity of sepsis is constantly increasing, with sepsis and septic shock remaining among the major causes of death worldwide. Hospital mortality of early septic shock in ICU patient of developed world is 18.8%[1] and hospital mortality in ICU patients of Bangladesh suffering from severe sepsis is 49·2%.[2]

1. Resident Physician, Department of Medicine, Chittagong Medical College Hospital, Chattogram-4203, Bangladesh.
2. Lecturer, Department of Pharmacology, Chittagong Medical College, Chattogram-4203, Bangladesh.
3. Professor, Department of Medicine, Chittagong Medical College Hospital, Chattogram-4203, Bangladesh.
4. Professor (Rtd), Department of Medicine, Chittagong Medical College Hospital, Chattogram-4203, Bangladesh.

Address of Correspondence: Dr. Sahed Uddin Ahmed, Resident Physician; Department of Medicine, Chittagong Medical College Hospital, Chattogram-4203, Bangladesh., Email: sahed51@gmail.com

Studies have found that one of the fundamental principles for the appropriate management of sepsis is early and accurate detection of the patients at high risk for death.[3] This is generally dependent on the application of scoring systems. Although various clinical biomarkers are widely explored like CRP, Procalcitonin, Lactate, CRP albumin ratio & IL-6,[4-7] only a few have been currently applied in the clinical practice.

Neutrophil lymphocytes ratio (NLR) has been the focus of several recent studies published as it is accessible, cheap and readily determined. The cause responsible for NLR elevations correlating with poor outcome in patients with sepsis remains unclear, although there are a variety of plausible explanations. One of the most convincing explanations is based primarily on the physiological link between neutrophilia and lymphopenia with systemic inflammation and stress. SOFA (sequential organ failure assessment)[8] score is derived from six organ system functions; two clinical observations including GCS and mean blood pressure and four biochemical parameters. Total SOFA score is 24. According to SOFA calculator, if an initial SOFA scores are 9-11, predicted mortality is 40-50%.The SOFA score is a simple, but effective method to describe organ dysfunction/failure in critically ill patients. International Sepsis guideline recommends 'SOFA score' as diagnostic and monitoring tool for sepsis patient of ICU. In this prospective observational study, we have sought to evaluate the predictive value of NLR and SOFA score in sepsis outcome in a consecutive series of adult patients at medicine department of a tertiary medical college hospital.

Methods:

This prospective observational study was conducted at inpatient Department of Medicine, Chittagong Medical College Hospital (CMCH) from August 2017 to May 2018. Patient who was admitted with sepsis in medicine ward or those who developed new episode of sepsis within the hospital was enrolled within 12 hours. Patient was diagnosed as sepsis on the basis of suspected or documented infection plus (a) two of qSOFA parameters out of three and or (b) two points increased out of twenty four points of SOFA score. Sepsis with other known comorbidity like; inflammatory arthritis, SLE, Sarcoidosis, CLD, ESRD, COPD with type II respiratory failure, heart failure, hematological malignancy, HIV infection, pregnancy, patient with receiving steroid and other immunosuppressive therapy within 4 week, any acute insult within last fourteen days; like severe trauma, acute pancreatitis, major abdominal or cardiothoracic surgery, acute stroke, acute coronary syndrome, major burn were excluded from the study after initial screening with history, clinical examination and relevant investigations. Differential diagnosis of sepsis like severe malaria, severe dengue, viral meningo-encephalitis, and diabetic emergency were excluded from history, clinical examination and relevant investigations. From all eligible subjects after getting consent clinical history was taken and clinical examination was done to elicit findings related to sepsis and its complication. With all aseptic precaution 10 cc of venous blood was collected and blood analyzers (Sysmex, Xn-1000, Company- Ves- Matic) were used to give automated counts of WBC, neutrophils, lymphocytes, monocytes, eosinophil and basophils. Finally it was rechecked by hematologist microscopically. NLR was calculated from differential count of WBC result. Admission SOFA score, association between all these parameters and NLR were done later. Data were arranged into two groups according to survival status or death. Sequential Organ Failure Assessment (SOFA) score was calculated at baseline on day 1 to assess the severity of illness. ICU referral and nephrology referral was noted. The total duration of hospital stay, ICU stay was recorded. All patients of the study were monitored until discharge or death to observe the outcome. The primary outcome was in-hospital mortality. Secondary outcomes were ICU referral and ICU stay.

All data were prospectively collected, coded and tabulated. Data were analyzed using descriptive statistical measurements; continuous variables were reported as mean values ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables were expressed as count and percentage. The ability of the variables to discriminate survivors from non-survivors was determined using receiver operating characteristic (ROC) curves. Multivariate logistic regression analysis to determine the independent predictors adjusted for the previously specified baseline covariates. Two- sided 5ØCÜ value < 0.05 was considered to represent a statistically significant difference. All analyses were performed by the IBM SPSS Statistics software version 23.0.

Results:

Effective sample size was 51. Among them 31 patients (60.78%) survived (Survivors Group) and the other 20 patients (39.22%) died (Non-survivors Group) in hospital (Table-I).

Table I : *Distribution of the patients by their survival and laboratory parameters*

CBC parameters	Patients group			P
	All patients (n=51)	Survivors (n=31)	Non-survivors (n=20)	value
WBC count (10^9/L)	15000 (12000-22000)	14000 (11660-22220)	18000 (13000-21000)	.122#
Neutrophil count (10^9/L)	12180 (9456-18000)	10356 (9300-17600)	15300 (11797-20160)	.024**
Lymphocyte count (10^9/L)	1530 (1172-2100)	1568 (1200-1568)	1350 (1060-1800)	.017**
NLR	8.6 (5.71-12.86)	7.7 (5.13-10.77)	11.06 (8.5-15.75)	.014**

Data are expressed as mean (SD), or median (interquartile range, IQR) as appropriate. WBC: white blood cell; NLR: neutrophil-to-lymphocyte ratio. # = Not significant by independent sample t test or Mann-Whitney test as appropriate. ** = Significant by Mann-Whitney test.

Value of SOFA score and NLR in predicting unfavorable outcome (Death):

ROC curves were constructed to evaluate the performance of NLR and SOFA in differentiating non-survivors from survivors, and the AUC for each indicator was compared (Figure I).

NLR had a modest power for predicting unfavorable outcome as suggested by AUC of 0.705 (95% CI: .556-.854), which was greater than that of baseline SOFA score (0.694).

NLR ≥8.9 was proposed as the optimal cutoff value, which provided a sensitivity of 75.0% and a specificity of 67.7% for predicting mortality in sepsis (Table II).

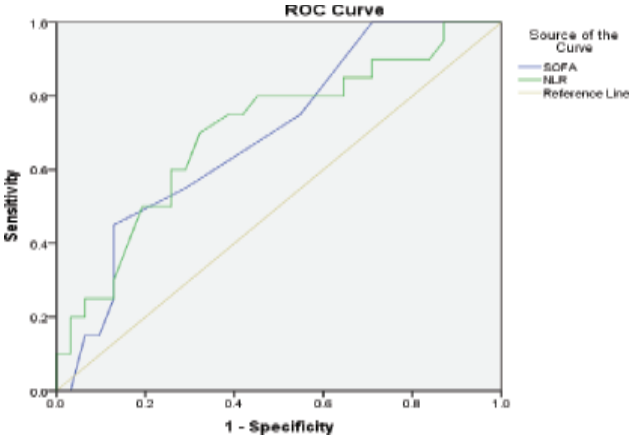

Fig.-1: Receiver operating characteristic (ROC) curves for SOFA score and NLR in predicting unfavorable outcome (mortality).

Table II : *Distribution of the patients by NLR category and survival*

Parameter: NLR category	Patients group All patients (n=51)	Survivors (n=31)	Non-survivors (n=20)	OR (95% CI)	P value
<8.9	30 (58.82%)	22 (71%)	8) (40%	3.66 (1.06-1.56)	0.028*
≥8.9	21 (29%)	9 (41.18%)	12 (60%)		

Data are expressed as number (%); *: Significant by Chi-square test. NLR: neutrophil- to-lymphocyte ratio; OR: Odds ratio; CI: Confidence interval

Table II shows that sepsis patients whose baseline NLR at admission was e”8.9 had 3.66 times morechance to death in comparison to the patients whose NLR was<8.9.

Table III : *Distribution of the patients by NLR category referral to ICU*

Parameter : NLR category	Referred to ICU No (n=27)	Yes (n=24)	OR (95% CI)	P value
<8.9	2 1 (77.8%)	9 (37.5%)	5.83 (1.71-9.90)	.004*
≥8.9	6 (22.2%)	15 (62.5%)		

Data are expressed as number (%); *: Significant by Chi-square test. NLR: neutrophil- to-lymphocyte ratio; OR: Odds ratio; CI: Confidence interval

Table III shows that sepsis patients whose baseline NLR at admission was ≥8.9 had 5.83 timesmore chance to require ICU support in comparison to the patients whose NLR was <8.9.

Table IV : *Independent predictors of unfavorable outcome by multivariate logistic regression analysis.*

Variables	Standard β value	Odds ratio	95% CI for OR		P value
			Upper	Lower	
Age	.058	1.060	.998	1.125	.057
Sex	-.669	.512	.087	3.005	.458
Illness duration	.190	1.209	.976	1.497	.082
Interval of bloodcollection	-.250	.779	.566	1.072	.125
DM	-.057	.945	.174	5.118	.947
COPD	.513	1.670	.087	32.076	.734
SOFA	.618	1.856	1.132	3.041	.014*
Neutrophil count	.000	1.000	1.000	1.000	.174
Lymphocyte count	.001	1.001	.999	1.002	.391
NLR	.305	1.357	1.017	1.810	.038*

The OR indicates the risk of obtaining unfavorable outcome. *Statistically significant.

Table IV shows that after adjusting for other variables NLR and SOFA remain as independent predictors of unfavorable outcome.

Discussion:

The main finding of our study was that the baseline NLR measured at the time of admission to medicine ward was associated with in-hospital mortality and NLR was able to accurately stratify patients in terms of mortality and ICU referral as like as baseline SOFA score. These findings remained significant after adjusting for several potential covariates, suggesting that increased NLR was independently associated with unfavorable outcome in patients with sepsis. Non-survivors had significantly higher qSOFA and SOFA score in comparison to the survivor group. This finding was similar to finding of American study.[9] No such study was found that included qSOFA and SOFA criteria in Bangladeshi literature.

Baseline laboratory parameters were revealed that NLR and neutrophil count were significantly higher and lymphocyte counts were significantly lower among non-survivors in comparison to survivors. Baseline NLR was 8.6 (5.71-12.86) in our study with significantly higher 11.06 (8.5-

15.75) among Non-survivors (p= 014), (Table VII). The average value of NLR in American healthy adults was found 2.15 (2.11- 2.19) with significant racial difference.[10] Normal NLR of Asian and Bangladeshi healthy adult population not yet studied. NLR of Bangladeshi type 2 DM patient was 1.56 (±.15), range was 1.23-1.74.[11] NLR of Bangladeshi sepsis patients not yet known.

The cause responsible for NLR elevations correlating with poor outcome in patients with sepsis remains unclear, although there are a variety of provable explanations. One of the most convincing explanations is based primarily on the physiological link between neutrophilia and lymphopenia with systemic inflammation and stress. The evolution of these leukocyte subpopulations may differ based on their respective role in the inflammatory response. Increased numbers of neutrophil imply that infection is not eradicate, which further induce depression of lymphocyte. Neutrophilia caused by demargination of neutrophils, delayed apoptosis of neutrophils and stimulation of stem cells by growth factors. Lymphocyte plays a key role in the regulation of inflammatory response, and lymphocytopenia appears as a consequence of lymphocyte margination and redistribution in the lymphatic system with accelerated apoptosis may lead to the immune system suppression and non- resolution of inflammation. The sustainability of infection,inflammation and the incomplete eradication of infection are responsible for the increase of neutrophils production by the bone marrow and decrease lymphocytes counts by apoptosis and others mechanisms. Therefore, the resulting increase in NLR may identify patients who are in a state of non-resolution of inflammation, along with concomitant decreased survival rates.

Zahorec R.[12] discovered the use of the NLR in septic and severe septic oncological ICU patients and

suggested that the ratio was associated with severity of disease. Zahorec investigated the differential white blood cell counts and the clinical course assessed by SOFA score in oncological ICU patients. They were found a correlation between the severity of clinical course and the grade of neutrophilia and lymphocytopenia was present. The author concluded that the ratio of neutrophil and lymphocyte counts was an easily measurable parameter which may express the severity of infections.

Receiver operating characteristic (ROC) curves for SOFA score and NLR in predicting unfavorable outcome (mortality) had shown that baseline NLR has higher sensitivity and specificity than baseline SOFA (AUC 0.705 Vs. 0.694 respectively). NLR e" 8.9 was proposed as the optimal cutoff value, which provided a sensitivity of 75.0% and a specificity of 67.7% for predicting mortality in sepsis, (Figure 3). Sepsis patients (n=21) of our study whose baseline NLR at admission was e"8.9 had 3.66 times more chance to death in comparison to the patients whose NLR was<8.9, (Table VII). Independent predictors of unfavorable outcome by multivariate logistic regression analysis had shown that both baseline NLR and baseline SOFA had significant predictive value. Varsha S. et al.[13] were compared neutrophil to lymphocyte count ratio and SOFA score as prognostic markers in the setting of emergency medicine in a prospective observational cohort study. On comparing NLR with SOFA score, NLR has 100% sensitivity and 67.24% specificity. A more recent study[14] showed that an initial value of NLR over ten could be correlated with an unfavourable prognosis, as assessed by the number of SIRS criteria, the presence of organ failures at admission. Xuan Liu et al.[15] prospectively enrolled adult patients with sepsis admitted to the ICU of the department of emergency, xinhua hospital, Shanghai; was found increased NLR (5ØCÜ = 0.000) in the non-survivors compared to patients that survived.

Moreover, a retrospective study[16] concluded that a value of NLR over seven on admission represented an independent increased mortality rate risk factor. Moreover, NLR was considered to be superior to other biomarkers such as CRP, leukocytes count or neutrophils count, as a predictor for bacteremia in patients admitted to emergency or intensive care units.[17] Other studies attempted to establish threshold values for NLR to predict the severity and outcome of the disease. In a large study by Hwang et al.[18]; with severe sepsis and septic shock, NLR measured at emergency department admission was independently associated with 28-day mortality. NLR was considered to be superior to other biomarkers such as CRP, leukocytes count or neutrophils count, as a predictor for bacteremia in patients admitted to emergency or intensive care units. [19]

Another prospective observational study[20] was conducted in the emergency department of the university hospital of Patras, Greece, based on consecutively enrolled patients suffering from sepsis of multiple origin. They found that NLR was positively correlated with the sepsis severity prognostic score on admission (SOFA, rs=0.497, p<0.001). In an Egyptian study; Okashah A et al.[21] highlighted NLR superiority regarding sensitivity, specificity to other parameters like lactate, CRP, neutrophils count, lymphocytes count, or leucocytes count. The same study showed the usefulness of NLR in prognostic evaluation by highlighting the statistically significant correlation with severity score SOFA (p=0.01). Bozkurt D et al.[22] performed a retrospective study investigating whether NLR has prognostic significance in patients suffered from AKI. To predict mortality, they showed that, level of 9.90 point for final NLR has 73% sensitivity and 87% specificity as compared to value below in ROC curve analysis (HR: 7.31, CI 3.36-15.91; p < 0.001).Sepsis patients of our study whose baseline NLR at admission was e"8.9 had 5.83 times more chance to require ICU support in comparison to the patients whose NLR was <8.9.NLR was also superior to SOFA score in predicting need for ICU referral for the sepsis patient as suggested by area under the curve. There was no similar study that NLR can predict ICU referral because most of the study done at ICU.

We observed, both baseline NLR and SOFA score remained statistically significant predictors of the severity of sepsis upon presentation of the patient to the hospital. Patients with NLR e" 8.9 had statistically significant (OR 3.66) in-hospital mortality (p<0.028) compared with those in NLR <8.9. After adjusted for other variables NLR and SOFA were remain as independent predictors of unfavorable outcome. However, in ROC curve analysis, NLR was superior to SOFA score to predict in-hospital mortality and ICU referral. Similar results were also found in the previous studies. In our study we demonstrated statistically significant relationship between baseline NLR and the sepsis prognostic scores SOFA upon medicine department presentation.

Conclusion:

The NLR is a biomarker easy to integrate in everyday clinical practice, as it is cost effective and easily calculated. The NLR could be a promising tool in the

initial assessment of patients with sepsis as we found significant relation between baseline NLR and SOFA score, the commonly used score of severity and prognosis of sepsis. In our opinion, the strength of the NLR is the possibility of implementing this parameter simply by using already available routine hematology count.

Limitations of the study:

Small sample size and selection of the cases from a tertiary level hospital might limit the generalize ability of the study results. Sepsis bundle management was not uniformly implemented in our setting that could have affected our result.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of Chittagong Medical College. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Acknowledgments:

The authors were grateful to the staffs of the Department of Medicine wards in Chittagong Medical College Hospital, Bangladesh.

References:

1. The ARISE Investigators and the ANZICS Clinical Trials Group. Goal-directed resuscitation for patients with early septic shock. New Eng J Med. 2014; 371(16):1496- 1506. https://doi.org/10.1056/NEJMoa1404380. PMid:25272316
2. Faruq MO, Ahsan ASMA, Nazim MU, Khatun UHS, Mannan MA, Jahan R et al. Implementation of Sepsis Bundles in Intensive Care Units of Bangladesh. Bangladesh Crit Care J. 2013 March; 1:8-17. https://doi.org/10.3329/bccj.v1i1.14359
3. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al. Surviving sepsis campaign. International Guidelines for Management of Severe Sepsis and Septic Shock. 2012; 583.
4. Devran O, Karakurt Z, Adýgüzel N, Güngör G, Özlem Yazýcýoðlu Moçin, Merih Kalamanoðlu Balcý et al. C-reactive protein as a predictor of mortality in patients affected with severe sepsis in intensive care unit. Multidisciplinary Respiratory Medicine 2012; 7:47. https://doi.org/10.4081/mrm.2012.634 https://doi.org/10.1186/2049-6958-7-47. PMid:23171626 PMCid:PMC3529702
5. Das S, Anand D, Ray S, Bhargava S, Manocha A, Kankra M et al. Role of Procalcitonin and high-sensitivity C-reactive protein in sepsis: a prospective study. Crit Care. 2011; 15(Suppl 3): P25. https://doi.org/10.1186/cc10394. PMCid:PMC3239268
6. Malmir J, Bolvardi E, Afzal Aghaee M. Serum lactate is a useful predictor of death in severe sepsis and Septic Shock. Rev Clin Med. 2014; 1(3):97-104.
7. Kim MH, Ahn JY, Song JE, Choi H, Ann HW, Kim JK et al. The C-Reactive Protein/Albumin Ratio as an Independent Predictor of Mortality in Patients with Severe Sepsis or Septic ShockTreated with Early Goal-Directed Therapy. PLoS ONE (2015) 10(7): e0132109. doi:10.1371/journal.pone.0132109. https://doi.org/10.1371/journal.pone.0132109. PMid:26158725 PMCid:PMC4497596
8. Jones A E, Trzeciak S and Jeffrey AK. The Sequential Organ Failure Assessment scores for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med. 2009 May; 37(5):1649- 54. https://doi.org/10.1097/CCM.0b013e31819def97. PMid:19325482 PMCid: PMC 2703722
9. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions forsepsis and septic shock (Sepsis-3). JAMA.2016 Feb 23; 315(8):801-810. https://doi.org/10.1001/jama.2016.0287. PMid:26903338 PMCid:PMC 4968574
10. Azab B, Camacho-Rivera M, Taioli E. Average Values and Racial Differences of Neutrophil Lymphocyte Ratio among a Nationally Representative Sample of United States Subjects. PLoS ONE.2014 9(11): e112361. doi:10.1371/journal.pone.0112361 https://doi.org/10.1371/journal.pone.0112361. PMid:25375150 PMCid:PMC4223021
11. Bhuiyan MMA, Islam MS, Ferdousi S, Borua D, Ghosh M, Akter S et al. Occurrence of coronary artery disease in patients with type 2 diabetes mellitus

can be predicted byneutrophil lymphocyte ratio. Bangladesh Med J. 2015 Sept; 44 (3):130-135. https://doi.org/10.3329/bmj.v44i3.27371

12. Zahorec R. Ratio of neutrophil to lymphocyte counts - rapid and simple parameter of systemic inflammation and stress in critically ill. Bratislavske Lekarske Listy. 2001; 102(1):5-14.
13. Varsha.S.Shinde, Vandana.A. Kakrani, V.S.Gokhale, S.K.Thombre, J.A.Landge. Comparison of neutrophil to lymphocyte count ratio, APACHE II score and SOFA score as prognostic markers in the setting of Emergency Medicine. International J. of Healthcare and Biomedical Research. July 2016; 04(4):46-51.
14. Orfanu A, Aramã V, Aramã ªS, et al. The diagnostic and prognostic role of neutrophil to lymphocyte count ratio in sepsis. BMC Infect Dis. 2016; 16(4):A5.
15. Xuan Liu, Yong Shen, Hairong Wang, Qinmin Ge, Aihua Fei, and Shuming Pan. Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Patients with Sepsis: A Prospective Observational Study. Mediators of Inflammation 2016; Article ID 8191254:8. https://doi.org/10.1155/2016/8191254 PMid:27110067 PMCid:PMC4823514
16. Terradas R, Grau S, Blanch J, et al. Eosinophil count and neutrophil-lymphocyte count ratio as prognostic markers in patients with bacteremia: a retrospective cohort study. PloS One. 2012; 7(8):e42860. https://doi.org/10.1371/journal.pone.0042860 PMid:22912753 PMCid:PMC3415420
17. Michal H, Beran O, Kaspøíková N, Chalupa P. Neutrophil to lymphocyte count ratio; as a biomarker of bacterial infections. Cent. Eur. J. Med. 2012; 7(2):258-261.. https://doi.org/10.2478/s11536-012-0002-3
18. Hwang Sy, Shin Tg, Jo Ij, et al. Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med 2017; 35: 234-39. https://doi.org/10.1016/j.ajem.2016.10.055. PMid:27806894
19. Orfanu A, Aramã V, Aramã ªS, et al. The diagnostic and prognostic role of neutrophil to lymphocyte count ratio in sepsis. BMC Infect Dis. 2016; 16(4):A5.
20. Velissaris D, Pantzaris ND, Bountouris P and Gogos C. Correlation between neutrophil-to- lymphocyte ratio and severity scores in septic patients upon hospital admission. A series of 50 patients. Rom. J. Intern. Med., 2018; 0(0):1-10. https://doi.org/10.2478/rjim-2018-0005. PMid:29427556
21. Okashah AS, El-Sawy MM, Beshay BN, Abd El-Raouf A. Ratio of Neutrophil to Lymphocyte counts as a simple marker for sepsis and severe sepsis in Intensive Care Unit. Res Opin Anesth Intensive Care. 2014; 2:39-45.
22. Bozkurt D, Kilic D, Kip T, Berktas M, Asli K, Fehmi A Bedside Alarmin: Neutrophil-to- Lymphocyte Ratio in Acute Kidney Injury. J Nephrol Ther. 2016; 6:251. https://doi.org/10.4172/2161-0959.1000251