ejpmr, 2019,6(11), 486-489

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

NEUTROPHIL TO LYMPHOCYTE RATIO VS PROCALCITONIN AS A MARKER FOR SEVERITY OF SEPSIS

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Article Received on 16/09/2019 **Article Revised on 07/10/2019** **Article Accepted on 28/10/2019**

ABSTRACT

Background: Severe sepsis and septic shock, are the major cause of emergency room admission and are associated with high morbidity and mortality worldwide. Similarly mortality rate of sepsis in asia found to be 40%, so sepsis is still the leading cause of death. Delayed identification and inadequate resuscitation in severe sepsis and septic shock leads to the high mortality. We compared the accuracy of the neutrophil-lymphocyte count ratio (N/L) to conventional inflammatory markers in patients admitted to the Intensive Care Unit. **Methods:** The current study was a retrospective study performed in KIMS hospital Bangalore. The study cohort consisted of 50 patients admitted to the medicine ICU/MICU. Patients were admitted to the ICU when they had manifest or imminent organ failure, especially circulatory, respiratory or renal failure All patients age more than 18 admitted with sepsis were included in the study. In the current study, patients with a known or probable immune deficiency were excluded, including patients with a haematological disease, patients treated with chemotherapy or immunosuppressive therapy including glucocorticoids. Procalcitonin levels and all routine investigations including investigations to find out source of sepsis were documented.Neutrophil/lymphocyte ratio was calculated, APACHE score and PCT were documented.all these parameters were compared based on outcome of the patient. **Results:** Significant differences in N/L ratio values were observed between sepsis and non-sepsis patients (12.3 vs. 2.4 ; P<0.001) The area under the ROC curve of the NLCR was 0.78. AUROC was significantly higher for PCT 0.86. APACHE 2 score correlated well with procalcitonin levels and the N/L ratio was found to be higher in the sepsis group than the non sepsis group. **Conclusion:** In the very busy emergency room where calculating APACHE 2 score or other scoring systems for sepsis is time consuming and expensive,other less expensive and time saving markers need to be implemented one such marker is the Neutrophil to lymphocyte ratio which can be calculated to assess the severity of sepsis but prognosis does not correlates well with serum procalcitonin levels and APACHE 2 score.

KEY WORDS: *Sepsis, Septic shock, procalcitonin, neutrophil lymphocyte ratio.*

1. INTRODUCTION

Diagnosing sepsis in severely ill patients remains a challenging task. In addition to the medical history and physical examination, laboratory markers of infection and inflammation play a major role in the final diagnosis. Currently, white blood cell (WBC) count, C-reactive protein (CRP) and procalcitonin (PCT) are commonly used to detect sepsis. However, increased levels of CRP can be found in various inflammatory conditions and, therefore, is of limited value in distinguishing infection from other causes of inflammation. Studies concerning PCT as a diagnostic tool for differentiating sepsis from systemic inflammatory response syndrome (SIRS) show conflicting results due to heterogeneity of study populations.

Following high mortality rates from sepsis, the Surviving Sepsis Campaign set out to standardise treatment through protocols. Early Goal Directed Therapy (EGDT) detailed interventions for treating patients with sepsis and their time-frame. After multiple permutations of the guidelines, and their latest revision in 2016, the current recommendations include time-critical administration of antimicrobial therapy and cardiovascular resuscitation (target within 1 hour and 3 hours, respectively).Initial studies showed improved in-hospital mortality for septic patients treated with EGDT. However, subsequent research including three large clinical trials and their associated meta-analysis have shown no significant improvement in patient outcome when using EGDT, undermining initial treatment strategies.

Despite the overwhelming burden of the disease, slow progress on treatment strategies has prompted calls for further research into sepsis. In particular, more knowledge is required of the factors that increase the risk

of death from sepsis, in order to guide treatment protocols and delivery of care, and ultimately reduce sepsis-associated mortality. The physiological immune response to infection and other stressful events is characterized by an increase in neutrophil count and a decrease in lymphocyte count. The increase in neutrophil count results from reduced apoptosis of neutrophils and rapid mobilization of neutrophils from a marginated pool within the bone marrow. The lymphocyte count is decreased by migration of activated lymphocytes to inflammatory tissues and by increased apoptosis of lymphocyte.The neutrophil-lymphocyte count ratio (NLCR) as a simple, rapid and cheap parameter of inflammation and stress in critically ill patients. More recently, the predictive value of the NLCR in patients with suspected bacteremia in the Emergency Department (ED) and the association between the NLCR and both short- and long-term outcome in critically ill patients was described.

2. METHODS

The current study was a retrospective study performed in KIMS hospital Bangalore. The study cohort consisted of 50 patients admitted to the medicine ICU/MICU. Patients were admitted to the ICU when they had manifest or imminent organ failure, especially circulatory, respiratory or renal failure All patients age more than 18 admitted with sepsis were included in the study. In the current study, patients with a known or probable immune deficiency were excluded, including patients with a haematological disease, patients treated with chemotherapy or immunosuppressive therapy including glucocorticoids.

Patients were divided into two groups depending on the presence or absence of sepsis. Sepsis was defined as the presence of two or more SIRS criteria (body temperature of more than 38°C or less than 36°C, heart rate of more than 90 beats per minute, respiratory rate of more than 20 breaths per minute, and WBC count below $4*10^9$/L or above $12*10^9$/L) and the presence of infection, confirmed by radiological or microbiological investigation. Patients with SIRS and high clinical suspicion of infection as determined by the treating physician, in the absence of confirmation of infection, were considered as having sepsis as well.

Of all patients, baseline clinical characteristics, as well as data concerning confirmation of infection, detected by microbiological investigation (positive cultures, serology, radiological investigation within 3 days after admission to the ICU as well as previous antibiotic use were collected from patient records.

Measurements of PCT, WBC count, neutrophil count and lymphocyte count were performed on blood samples collected at admission to the ICU.PCT levels were measured using a commercially available sensitive immunoluminometric assay. WBC count, neutrophil count and lymphocyte count were determined. The NLCR was calculated by dividing the neutrophil count through the lymphocyte count (normal value 0.7 and 3.5). A PCT level above 100 ng/ml or below 0.02 ng/ml were documented. APACHE 2 score was calculated as a means of control.

3. RESULTS

50 patients diagnosed with sepsis and septic shock were included in the study ,out of the 50 patients 24 were male and 26 were female, 28 of the 50 patients died 18 male and 10 female.50 patients without sepsis were taken as controls, serum procalcitonin were noted.APACHE 2 score was calculated as control.

Data collection

The data collected from the patients were as follows: basic data of patients, including age, sex, mean time to onset, source of infection, etiology, and underlying diseases; N/L ratio was calculated ,the procalcitonin values obtained from all the patients at 0 h after admission to the ICU. The APACHE II scores which were pooled and calculated.

Outcome measures

The correlations of N/L ratio, procalcitonin levels and the APACHE II were analyzed among the patients in the two groups.

Statistical analysis

Measurement data were represented as mean ± standard deviation (x ±s); the comparisons between the groups were made by the t-test, and the comparisons within the same group. Data were represented as percentages, and the comparisons between the groups were made with the chi square test. Pearson correlation analysis was utilized for detection of the prognostic correlations and APACHE II score correlations. A P value of less than 0.05 was considered statistically significant.

Table 1.: basic data of patients.

VARIABLES	SEPSIS GROUP	NON SEPSIS GROUP
CASE	50	50
AGE	58.3+/-6.1	52+/-4.2
GENDER(M/F)	24/26	21/29

Majority of the patients in study /group and non sepsis group had pulmonary disorder(54%),followed by GI (18%), urinary tract infections(16%), skin and soft tissue(4%)and CNS(8%) respectively in the sepsis group. (table 2)

Table 2: Etiology of sepsis.

ETIOLOGY	SEPSIS GROUP	NON SEPSIS GROUP
PULMONARY	27	28
ABDOMINAL	9	12
URINARY TRACT	8	5
SKIN AND SOFT TISSUE	2	3
CNS	4	2
TIME TO ONSET(DAYS)	4+/-2.0	6+/-2.0

Table 3: Statistical analysis of N/L ratio, PCT, APACHE 2 score in the sepsis and non sepsis group.

VARIABLE	SEPSIS (mean+/-)SD	NON SEPSIS (mean+/-)SD
N/L RATIO	12.3	2.4
PROCALCITONIN	21.6	1.3
APACHE 2 SCORE	21	4

It was found that the mean N/L ratio was much higher in patients with sepsis than patients in the non sepsis group, but did not correlate well with the procalcitonin levels and APACHE 2 scores

Table 4: The correlation of serum lactate, procalcitonin and APACHE 2 scores.

VARIABLES	CORRELATION COEFFICIENT	P VALUE
N/L RATIO	0.72	0.022
PROCALCITONIN	0.88	0.012
APACHE 2	0.84	0.010

Serum procalcitonin levels and APACHE 2 scores had better correlation with severity of sepsis than the neutrophil lymphocyte ratio with a correlation coefficient of 0.72, 0.88 and 0.84 for N/L ratio, procalcitonin and APACHE 2 score.

4. DISCUSSION

Septic shock is a clinical complication with high mortality caused by the worsening health conditions in patients with sepsis, primarily as the result of the interactions between bacterial infection and immune defense mechanisms. Currently, although growing advances have made in medical treatment, the mortality of septic shock remains high. Therefore, assessment of the severity of sepsis in the patients encourages early intervention in a timely manner, reducing the mortality of the patients.

The APACHE II score is one of the measures for assessing the severity of diseases in critically ill patients, and is extensively used in clinical practice. Monitoring the APACHE II score can not only assess the patient's conditions, but also predict the mortality of the patients. The results of the present study demonstrated that the mean APACHE II score in the survival control group was significantly lower than that in the death group ($P<0.05$).

Moreover, the APACHE II score was negatively correlated with the prognosis of patients, with lower APACHE II scores indicating better prognosis. This may be due to the fact that the APACHE II score is involved in a sea of clinically physiological and laboratory indicators, and the patients with septic shock frequently have a variety of underlying diseases, leading to hypoxia, acidosis, and electrolyte disturbances. All these are associated with the abnormality in the indicators, and concurrently suggest that more severe organ dysfunction indicates worse prognosis. The results were basically similar to those in the previous reports.

Multiple studies worldwide have shown that procalcitonin can effectively induce the effect of ant-infection in critically ill patients. Besides, procalcitonin can be used as an early indicator for the diagnosis and assessment of bacterial infectious diseases. The present study found that, as compared to the death group, the procalcitonin levels decreased significantly among the patients in the survival control group; over time, the procalcitonin showed a dropping trend; in addition, the procalcitonin level was negatively correlated with prognosis of the patients, but positively correlated with the APACHE II score. It suggests higher procalcitonin level indicating worse prognosis.

APACHE 2 scores and procalcitonin levels predicting the mortality of patients with septic shock on the ROC curves showed the areas under the curves of greater than 0.5, with significant differences. In the present study, the area under the curve was calculated as including N/L ratio and procalcitonin levels of all patients, bur no subgroup analysis was performed.

In conclusion, monitoring N/L ratio at admission, is not a better indicator than serum procalcitonin and APACHE 2 score in sepsis and septic shock.

5. CONCLUSION

In the very busy emergency room where calculating APACHE 2 score or other scoring systems for sepsis is time consuming and expensive, Neutrophil to lymphocyte ratio can be calculated to assess the severity of sepsis but prognosis does not correlates well with serum procalcitonin levels and APACHE 2 score

6. ACKNOWLEDGEMENT

We extend our gratitude to all the faculty members of the Department of General medicine and all the other supporting departments and the management for giving their valuable opinion and suggestions during discussion and extending their help in working towards this article. We extend our gratefulness to all the patients. A special thanks goes to Dr Manjunath, Professor and HOD, department of medicine for giving his support in making this study a success.

Source of suppost in form of grants: nil
Conflicts of interest: nil

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