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ORIGINAL RESEARCH ARTICLE

To Study Neutrophil –Lymphocyte Ratio as an Independent Risk Factor for Predicting Acute Kidney Injury in Patient with Sepsis

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Abstract: Introduction: Acute kidney injury (AKI) is a common sequel of sepsis and is associated with unacceptably high morbidity and mortality, prolonged hospital stay, and increased costs of care among critically ill patients. AKI is frequent in hospitalized patients and its incidence is higher in critically ill patients, in whom the leading cause of AKI is sepsis, substantiated by multiple cohorts. Septic-AKI patients have distinct characteristics than non-septic AKI, that is higher severity scores at admission, more non-renal organ failure and requirement of vasopressors and mechanical ventilation.**Aim and Objective**: To obtain neutrophil-lymphocyte ratio in sepsis with acute kidney injury patients and predict it as an independent risk factor for sepsis induced acute kidney injury and to compare value of neutrophil-lymphocyte ratio with Other inflammatory markers like total WBC count and c-reactive protein etc.**Material and Methods**: This was an observational – comparative study started from Feb 2020 till achieving sample size and two months for data analysis and conclusion at General Medicine department wards of SMS Hospital and attached group of Hospitals, Jaipur, Rajasthan, India. The study included a Sample size of 30 of each group (sepsis with aki and sepsis without aki) as a previous study shows minimal detectable difference of mean 2.63, SD-1.88 for 80% power and 0.05 alfa error.**Result**: The study included Sample size of 30 Patients. Here we found that majority 53.3% patients were smoker followed by 36.6% patient in group A. In group B, 60% patients were smoker followed by 36.6% of alcoholic. Here we found that majority 53.3% patients were smoker followed by 36.6% patient in group A. In group B, 60% patients were smoker followed by 36.6% of alcoholic. There was no significant difference as p value was >0.05. Here we found that majority of patients in group A was of HTN (56.6%) followed by 33.3% of COPD.**Conclusion**: We have found that cellular immunity and inflammation play a central role in prediction of AKI in sepsis. We considered that baseline NLR might be used to early diagnosis of AKI in sepsis if more prospective studies with larger sample sizes would be needed to confirm. We suggested that NLR, APACHE II and invasive mechanical ventilation appeared to be a risk factor for development of AKI in sepsis.

Keywords: Neutrophil –Lymphocyte Ratio, Independent Risk Factor, Acute Kidney Injury, Sepsis.

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Introduction

Acute kidney injury (AKI) is a common sequel of sepsis and is associated with unacceptably high morbidity and mortality, prolonged hospital stay, and increased costs of care among critically ill patients.[1] AKI is currently defined by a rise of Serum creatinine from baseline by at least 0.3 mg/dL within 48 h or at least 50% higher than

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baseline within 1 week, or a reduction in urine output to less than 0.5 mL/kg per hour for longer than 6 h. AKI is frequent in hospitalized patients and its incidence is higher in critically ill patients, in whom the leading cause of AKI is sepsis, substantiated by multiple cohorts.[2,3]

Sepsis is the systemic inflammatory response to an infectious insult, which often results in multiple organ dysfunction. Sepsis, a serious and life-threatening syndrome designated as immune disorder and organ dysfunction subsequent to the host response to infection, is notoriously known for its favour to patients in the intensive care unit (ICU).[4]

Septic-AKI patients have distinct characteristics than non-septic AKI, that is higher severity scores at admission, more non-renal organ failure and requirement of vasopressors and mechanical ventilation.[3,5]

Postoperative AKI and its stages are independent risk factors for the prognosis of surgical patients.[6] In addition, a large number of studies have reported that AKI significantly increases the risk of chronic renal insufficiency and end-stage kidney disease.[7]

Neutrophil–lymphocyte ratio (NLR) is an indicator of systemic inflammation, calculated easily from complete blood count.[8] Some studies showed that NLR is promising marker in predicting bacteremia in patients with emergency medical admissions. NLR was used as prognostic marker in patient with bacteremia.[9] The neutrophil to lymphocyte ratio (N/L ratio) have been associated with AKI in the emergency setting, sepsis, contrast induced-AKI, cardiovascular surgery and abdominal surgery.[10] These are easily calculated, effective and low-cost markers of systemic inflammation which might be promising in AKI patients. The prognostic ability of the neutrophils to lymphocytes ratio (N/L ratio) has not previously been evaluated in septic-AKI.

The aim of this study was to evaluate the prognostic ability of N/L ratio at admission in septic-AKI patients admitted to an intensive care unit (ICU). We aimed to investigate whether NLR is a predictor of AKI in patients with septic shock.

Material and method

This was an observational – comparative study started from Feb 2020 till achieving sample size and two months for data analysis and conclusion at General Medicine department wards of SMS Hospital and attached group of Hospitals, Jaipur, Rajasthan, India. The study included a Sample size of 30 of each group (sepsis with aki and sepsis without aki) as a previous study shows minimal detectable difference of mean 2.63, SD-1.88 for 80% power and 0.05 alfa error, who went through inclusion and exclusion criteria are included in this study. **Inclusion criteria:- 1.** Individuals giving written informed consent to be a part of the study 2. Age more than 18 years 3. Patient with first episode of sepsis. **Exclusion criteria**:- 1. Renal dysfunction on admission **2.** Renal replacement therapy was used at the start of the study 3. Patients with hematological disease, receiving chemotherapy or glucocorticoids 4. patients in whom care was withdrawn within 6 h of onset of septic shock 5. being exposed to radiocontrast dye or nephrotoxic drugs (aminoglycoside, colistin and amphotericin) within at least one week before the admission to ICU.

Result

In our study we found that majority (43.3%) patients of 56-70 years followed by 36.6% patients in 41-55 years were in group A. In group B, 43.3% patients in 56-70 years age group followed by 40% patients in 41-55 years age group. The mean age for group A was 51.2 years and for group B it was 52.3years. Here we found that majority 73.3% and 66.6% patients were male in group A and group B respectively.

Table 1: Distribution of cases according to risk factors.

Risk Factors	Group A		Group B		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Alcoholic	11	36.66667	11	36.66667	1
Smoker	16	53.33333	18	60	0.6
None	6	20	8	26.66667	0.54

Here we found that majority 53.3% patients were smoker followed by 36.6% patient in group A. In group B, 60% patients were smoker followed by 36.6% of alcoholic. There was no significant difference as p value was >0.05. Here we found that majority of patients in group A was of HTN (56.6%) followed by 33.3% of COPD. In group B, 33.3% patients were of HTN and T2DM each.Here we found that mean SBP, DBP, RR/min and PR/min for group A was 129.2, 88.26,20.3 and 89.2 respectively. For group B, mean SBP, DBP, RR/min and PR/min was 127.4, 79.2, 20.4 and 88.6 respectively.

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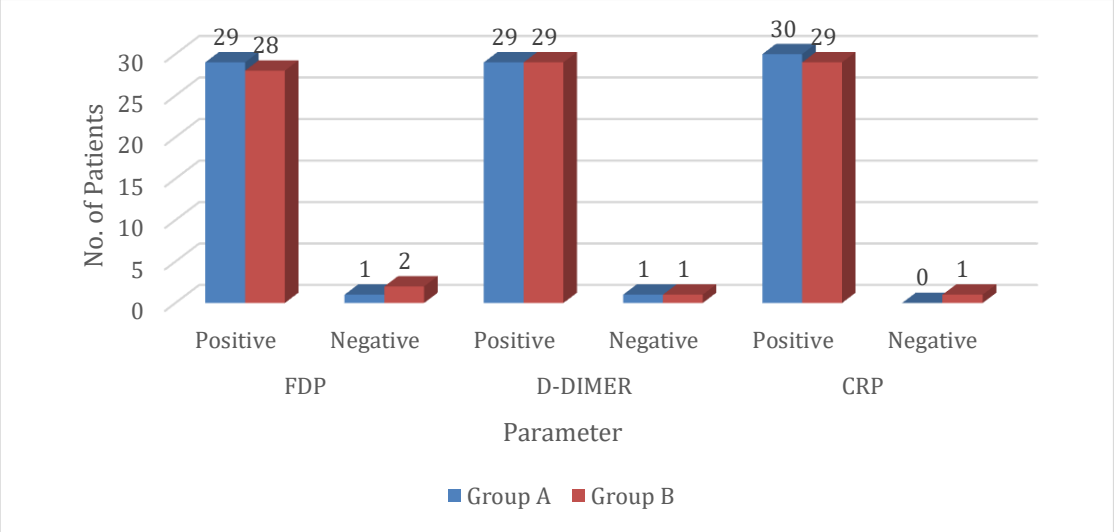


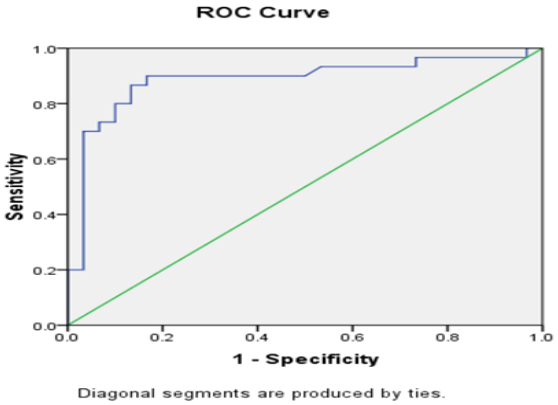
Graph 1: Distribution of cases according to FDP, D-DIMER and CRP.

Here we found that 96.6%, 96.6% and 100% patient in group A was FDP, D-Dimer and CRP positive. In group B, 93.3%, 96.6% and 96.6% patients were FDP, D-Dimer and CRP positive. There was no significant difference as p value was >0.05. we found that mean Hb, TLC and Platelets for group A was 12.1, 19.2 and 1.85 respectively. For group B mean Hb, TLC and Platelets was 12.2, 20.49, and 1.19 respectively. Here we found that mean NLR for group A was 9.31 and for group B it was 16.53. Mean PCV and ESR for group A was 42.3 and 55.3 respectively. For group B mean PCV and ESR was 47.4 and 43.8 respectively.

Table 2: Risk factors for development of AKI in patients with sepsis: multiple logistic regression analysis.

Parameter	OR (95% CI)	P-Value
Age	1.0068 (0.93-1.08)	0.86
Apache Score	0.91(0.68-1.22)	0.55
NLR	0.68(0.57-0.82)	0.0001
ACEIS/ARBS	3.01(0.91-9.90)	0.06
DOMV	0.54(0.36-0.81)	0.002

Here we found multiple logistic regression analysis on age, apache score, NLR, ACEIS/ARBS and DOMV. Here we found that mean blood urea, serum creatinine and serum albumin at day 1 and at day 7 for group A and group B. The p value was significant for blood urea, serum creatinine at day 7. Here we found that mean PT-INR for group A was 1.09 and for group B it was 1.32. Mean Procalcitonin for group A was 2.15 and for group B it was 3.28. we found that mean ALT for group A was 69.3 and for group B it was 63.6. Mean AST for group A was 71.7 and for group B it was 64.7.



Graph 2: ROC for prediction of AKI with sepsis with NLR.

Here we found roc for prediction of patients in AKI with sepsis. The AUB was 0.88 with p value

<0.001. The cut-off NLR value was 10.2. The sensitivity was 90% and specificity was 83.3%. Here we found that mean APACHE 2 score was 20.9 and 22.87 for group A and group B respectively. Here we found that mean DOMV for group A was 4.5 and for group B 5.36. Here we found that ACEIS/ARBS was positive for 53.3% and 30% in group A and group B respectively. Here we found that mean urine output for group A at day 1 was 1366.6 and for group B it was 1419.6. At day 7, mean urine output for group A was 1295 and for group B it was 601.6.

Discussion

The study showed mainly that, within 24 h after ICU admission, calculated NLR is powerful and independent predictor of sepsis-related-AKI in patient with sepsis. Patients with sepsis-related-AKI had higher NLR levels than patients without sepsis-related-AKI. Secondly, duration of invasive MV, APACHE II score may be an independent predictor of sepsis-related-AKI. Sepsis is life threatening organ dysfunction caused by the host's harmful response to infection. Patients with AKI significantly increased sepsis mortality. Studies have shown that sepsis is associated with 50% of AKI, and up to 60% of sepsis patients develop organ dysfunction including AKI. Mechanism of sepsis-induced AKI is that deleterious inflammatory cascade of sepsis causes kidney damage.[11] Several studies have shown that NLR is a predictor of AKI occurrence in patients with sepsis. They showed that NLR ≥ 9.11 in sepsis had a high risk of AKI occurrence.[12]

We found that majority 53.3% patients were smoker followed by 36.6% patient in group A. In group B, 60% patients were smoker followed by 36.6% of alcoholic. There was no significant difference as p value was >0.05. Song M et al found that the Forty-eight percent were past or current smokers and 70% were overweight/obese.

We found that 96.6%, 96.6% and 100% patient in group A was FDP, D-Dimer and CRP positive. In group B, 93.3%, 96.6% and 96.6% patients were FDP, D-Dimer and CRP positive. There was no significant difference as p value was >0.05. Mean ALT for group A was 69.3 and for group B it was 63.6. Mean AST for group A was 71.7 and for group B it was 64.7. The p value was non significant for both the parameter.Yilmaz H et al[13] found that there was no difference in albumin, CRP, WBC between Group 1 and Group 2.

We found multiple logistic regression analysis on age, apache score, NLR, ACEIS/ARBS and DOMV. Gameiro J et al[14] found that the N/LP ratio at admission was associated with in-hospital mortality in septic-AKI patients (31.59 ± 126.8 vs 13.66 ± 22.64, p = 0.028). MEHTA, et al[15] found that independent risk factors for AKI included young age and presence of shock, sepsis and need for mechanical ventilation (P<0.001).

Yilmaz H et al[13] used Multivariate logistic regression was used to assess possible risk factors for AKI occurrence. Four variables were selected for multivariate regression: APACHE II, NLR, use of ACE or ARB, duration of invasive MV. Age was added to multivariate logistic analysis. After adjustment for confounders, the development of AKI was independently associated with NLR (OR: 3.25, CI: 2.72–4.19, p50.001), APACHE II (OR: 1.72 CI: 1.61–1.92, p ¼ 0.038) and duration of invasive MV (OR: 1.28, per one hour, CI: 1.07–1.41, p ¼ 0.048).

We found roc for prediction of patients in AKI with sepsis. The AUB was 0.88 with p value <0.001. The cutoff NLR value was 10.2. The sensitivity was 90% and specificity was 83.3%. Brio G M C et al[16] found that the analysis of the ROC curve showed that the best cutoff point for NLR, with 76.19% sensitivity and 48.44% specificity, was 1.98. Tonyali et al[17] found a cutoff point of 3.18 for NLR in patients in the postoperative period of partial or radical nephrectomy, and for Yilmaz et al[18], who worked with cases of severe sepsis and acute kidney injury, the cutoff point for NLR was 10.5. Jian Bin et al[19] found that ROC curves analysis with occurrence of AKI was used to determine the optimal cut-off value of NLR. The value of NLR at the maximum value of the Youden index is taken as the optimal cut-off point. The optimal cut-off value of NLR was 8.380 [sensitivity of 82.14% and specificity of 43.43%, area under the curve = 0.634, 95%CI: 0.563-0.705, P = 0.0004].

Conclusion

Baseline NLR would be a strong indicator for prediction of AKI in patients with sepsis. We suggested that cellular immunity and inflammation play a central role in prediction of AKI in sepsis. We considered that baseline NLR might be used to early diagnosis of AKI in sepsis if more prospective studies with larger sample sizes would be needed to confirm. We suggested that NLR, APACHE II and invasive mechanical ventilation appeared to be a risk factor for development of AKI in sepsis.

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